Onsen in Japan

Balneology in Europe

What can we learn from each other ?
Research and tradition

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Japan and Germany

- Long tradition of healing with water
- (Economic) success by adaption to changes and challenges

- Nature (forest, climate) as healing factor (shinrin-yoku)
- Similar mineral waters (high CO2)

- Higher water temperatures in Japan
- Health resorts with proven quality in Germany

Summary of this lecture

- I want to show some results of recent research and discuss possible solutions and cooperation
    - Balneotherapy and CO2 in peripheral artrial diesease
    - Hyperthermic baths and Sauna
    - Thermoneutral baths with and without exercise
    - Forest medicine shinrin-yoku
    - Health resorts in Germany
    - Drinking mineral waters and dementia
        - Silicea, Lithium Magnesium,

Balneotherapy in Peripheral Arterial Disease

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CO2 baths: physiologic basis

- Increase of cutaneous blood flow, peripheral vasodilation
- Catecholamine plasma levels decrease
- Decreased sympathetic an increased parasympathetic activity
- Thermal sensation score increases (blockage of cold receptors?)
- Bohr effect (rightward shift in O_2 - dissociation curve)
- NO-elevation, activation NO-cGMP pathway
- Induction of local VEGF

Carbon dioxide balneotherapy and cardiovascular disease. Pagourelias ED et al. Int J Biometeorol. 2011 Sep;55(5):657-63.

Carbon dioxide-rich water bathing enhances collateral blood flow in ischemic hindlimb via mobilization of endothelial progenitor cells and activation of NO-cGMP system. Irie H, Circulation. 2005 Mar 29;111(12):1523-9.

Effects of immersion in water containing high concentrations of CO2 (CO2-water) at thermoneutral on thermoregulation and heart rate variability in humans. Sato M Int J Biometeorol. 2009 Jan;53(1):25-30

Balneotherapy in Peripheral Arterial Disease

- **Carbondioxid baths**, water and gas, thermoneutral
  - 4 RCT, 2 blinded, 4 OS
- **Radon, water, hyperthermic**, 1 RCT, n=128, diabetes)
- **Waon Sauna** (2 OS, n=20, n=21)

- Hydrotherapy (Contrast showers 1 OS n=20)
- Sulphur baths (homcysteine 1 RCT, not blinded n=40)
- Galvanic baths (1 CT, not randomized, not blinded, n=111)
- Hypnosis (1 OS, n=18)

All trials show positive results

Natural CO_2 gas baths

- RCT, n=62, intermittent claudication
  (100-500 meters, moderate Fontaine stage II)
- constant temperature of 30°C on pre-humidified skin.
- 18 consecutive days of (Spa of Royat, France)
  - CO2 gas treatment
  - placebo (air).

Figure 1: Treatment (pre-humidified skin)
Bath of tap water for 10 minutes at a temperature of 34-35°C

Figure 2: Treatment (CO_2 or placebo)
Application of CO_2 or placebo for 35 minutes over 80% of the body surface

Natural CO_2 gas baths

CO_2 gas treatment after 18 days with significant increase in

- total distance walked (+ 131 meters, 66%; p = 0.001)
- pain-free distance (+ 81 meters, 73%; p = 0.02)
- improvement maintained after 3 and 12 months
- systolic pressure index (ABI) increased by 37% (p = 0.001) 1 min after treadmill walking
- ABI recovery time decreased by 38% (p = 0.002).
- increase in systolic pressure of the great toe (13%; p < 0.0001), in baseline pO2 (20%; p = 0.01) and in vasomotion (78%; p = 0.001)

No significant change was observed in the placebo group.

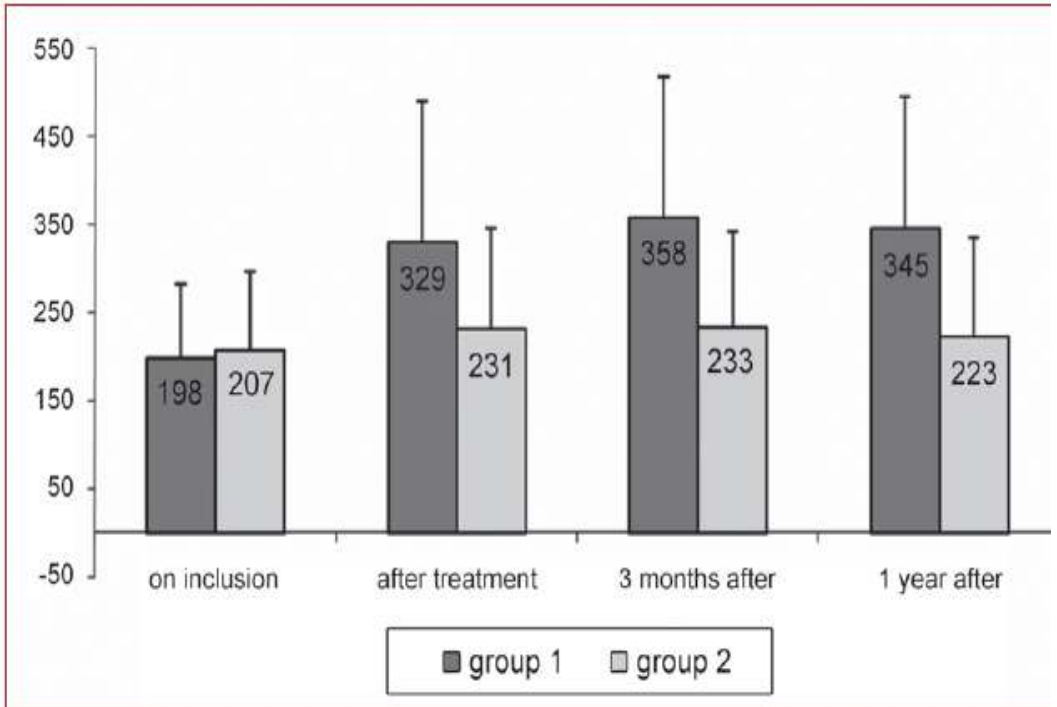

Figure 3: Changes in total walking distance (mean value ± SD, meters) Total distance on inclusion is mean value for each patient of measurements recorded during treadmill tests 1 and 2 before randomisation. p = 0.001 for group 1, before / after treatment at each measuring time intergroup p values = 0.001 after treatment at each measuring time

Clinical and microcirculatory effects of transcutaneous CO2 therapy in intermittent claudication. Randomized double-blind clinical trial with a parallel design. Fabry R, Monnet P, Schmidt J, Lusson JR, Carpentier PH, Baguet JC, Dubray C. Vasa. 2009 Aug;38(3):213-24.

Effects of hyperthermia on depression

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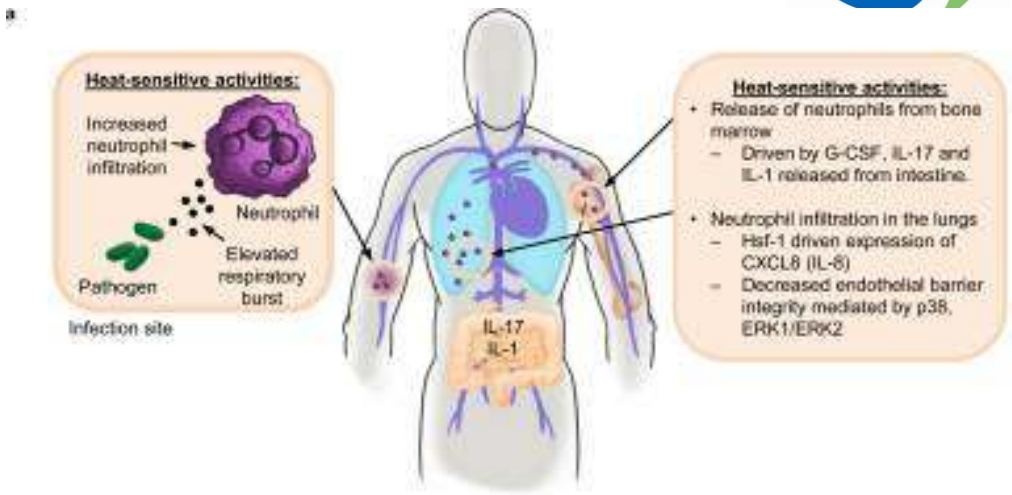
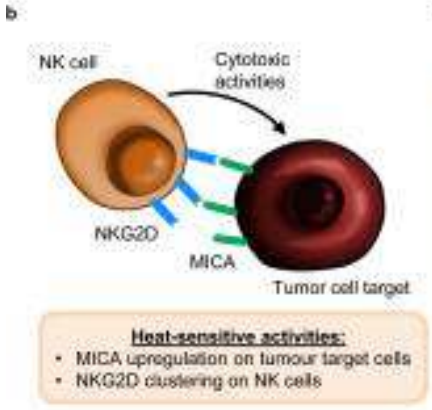
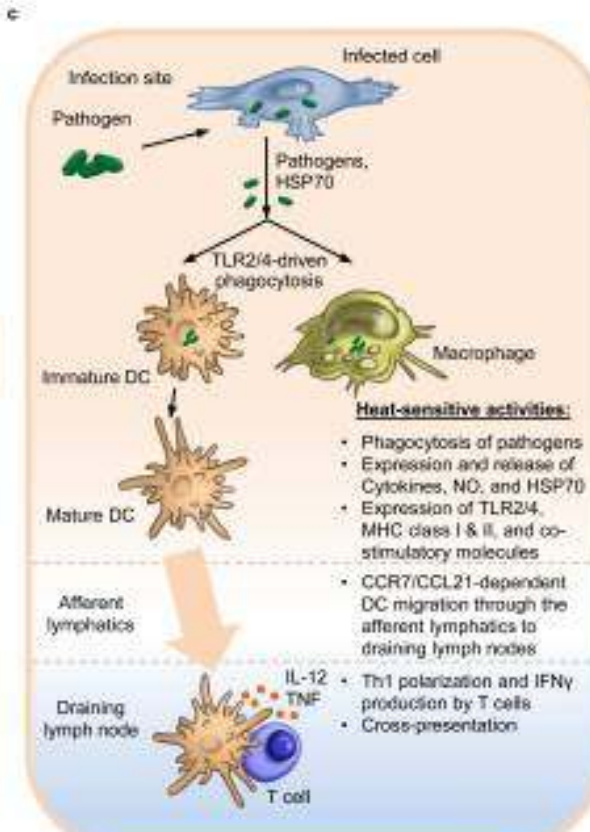
Hyperthermia effects

- Acitivates immune system
  - Heat shock proteins
- Regulates vegetative system
- Affects sleep

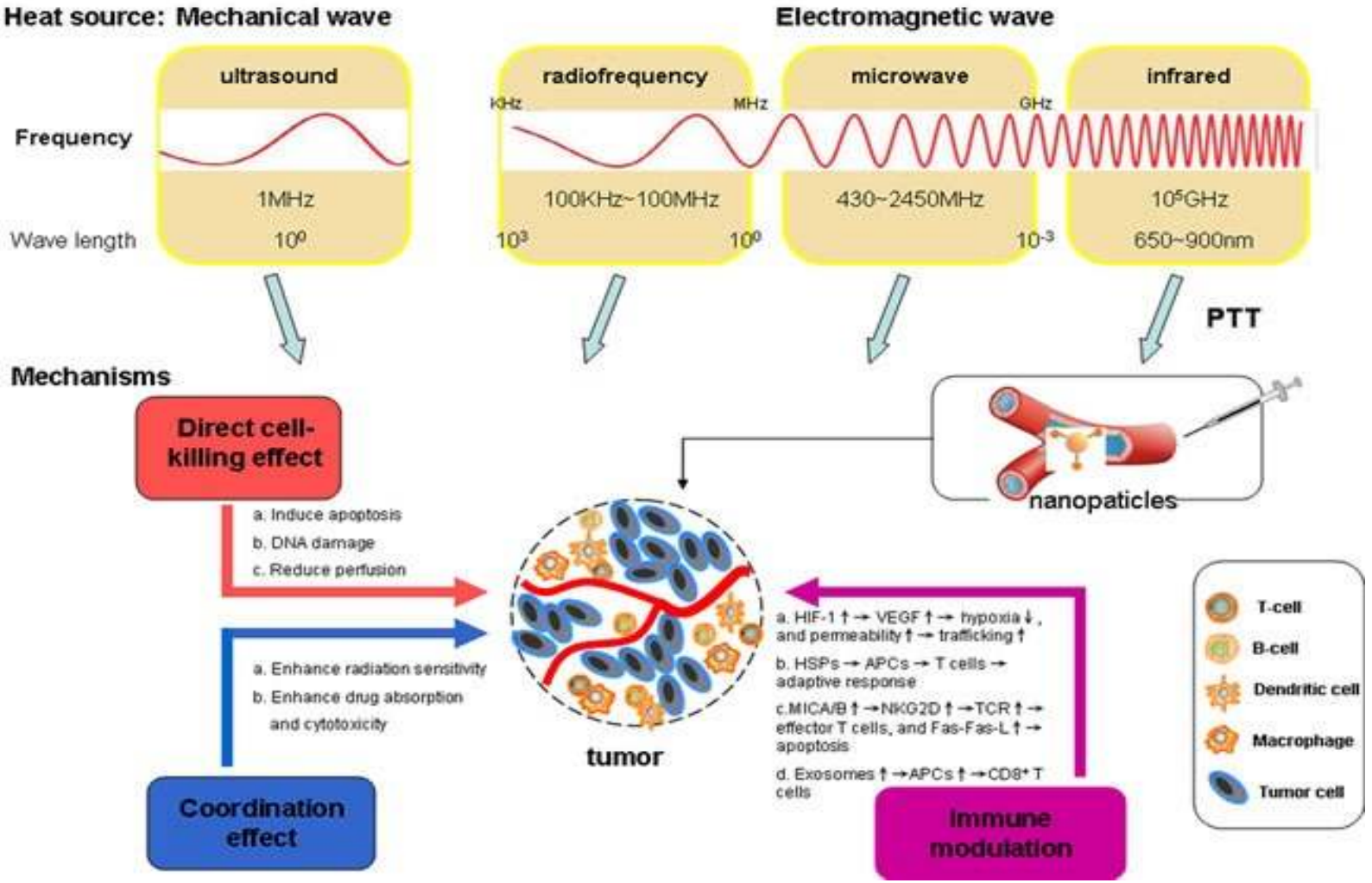






https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4786079/figure/F2/?report=objectonly

Hyperthermia effects in oncology



Oncotarget 2016 Aug 30;7(35) : 57367-57378. Local hypert-hermia in head and neck cancer: mechanism, application and advance. Gao S

Heat sources used for hyperthermia purposes and different mechanisms induced by locally heating tumors. The mechanism of killing tumor cells *via* the following aspects: (1) Direct cell-killing effects of HT alone (red); (2) Anti-neoplastic effect coordinated with radiotherapy and chemotherapy (blue); (3) Immune modulation (purple).

Hyperthermic Baths (HTB)

- Head-out-of-water-immersion in a 40°C pool
- duration until discomfort (30 minutes)
  - Mean duration 22.6 (± 3.5) min
- Afterwards wrapped in warm blankets with 2 hot water bottles for at least 30 minutes
- 4 weeks with 2 interventions per week

Keidel-Bad Freiburg

HTB and Depression

- Non-controlled study
- 20 depressive patients
- Improvement in the 21-item Hamilton Depression Scale (HAMD) after five baths.

Schaper LC. Wiederholte Hyperthermiebehandlung durch Überwärmungsbäder bei Patienten mit depressiven Störungen: Effekte auf die Produktion von Interleukin-6 sowie auf die mittlere Körpertemperatur und den psychopathologischen Befund. 1996.

- Non-controlled study in depressive patients
- Effects on Heart Rate Variability (HRV)

Gödl, R. 2000. "Veränderungen Der Autonomen Regulation Durch Überwärmungsbadtherapie Bei Patienten Mit Depressiven Störungen. (Unpublished Doctoral Dissertation, University of Graz, Austria)." Medizinischen Fakultät der Karl-Franzens-Universität Graz.

HTB vs sham light treatment

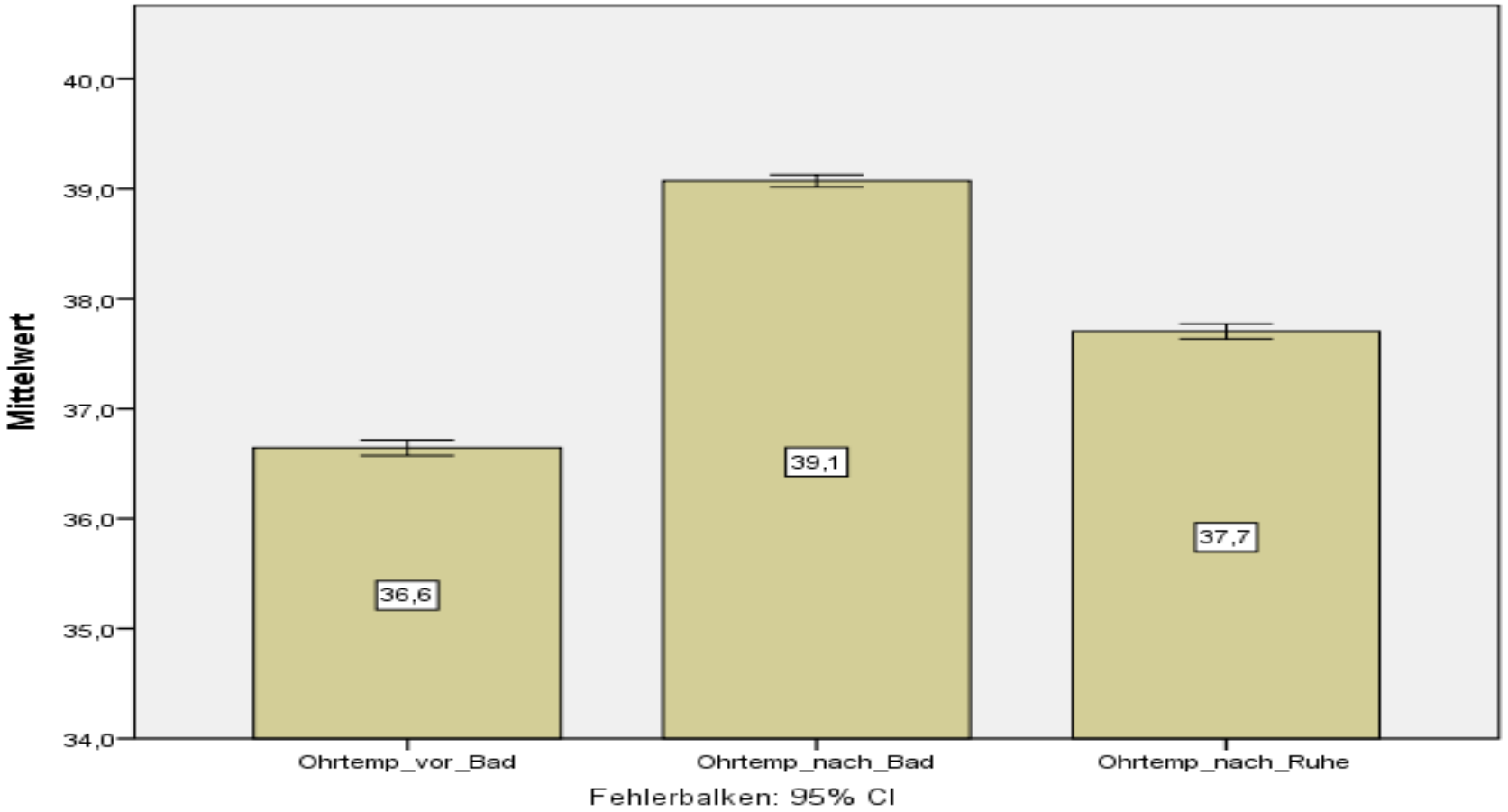
- Pilot study, parallel-group, randomized controlled trial
- 36 depressed patients with Hamilton Scale for Depression (HAM-D) total score **≥ 18** (mean HAM-D 22.4)
  - 17 HTB
  - 19 sham green light
    - < 400 Lux by an LED, < 40 min in a sitting position

Naumann J, Sadaghiani C, Grebe J, Kaiffel S, Huber R. Effects of hyperthermic baths on depression, sleep and heart rate variability in patients with depressive disorder: a randomized controlled pilot trial BMC Complement Altern Med. 2017 Mar 28;17(1):172

HTB Core body temperature

(Ear thermometer after ca. 22 min)

- Before bath 36.6°C
- Directly after bath 39.1°C (mean change 2.43 K)
- after rest 37.7°C (mean change 1.06 K)



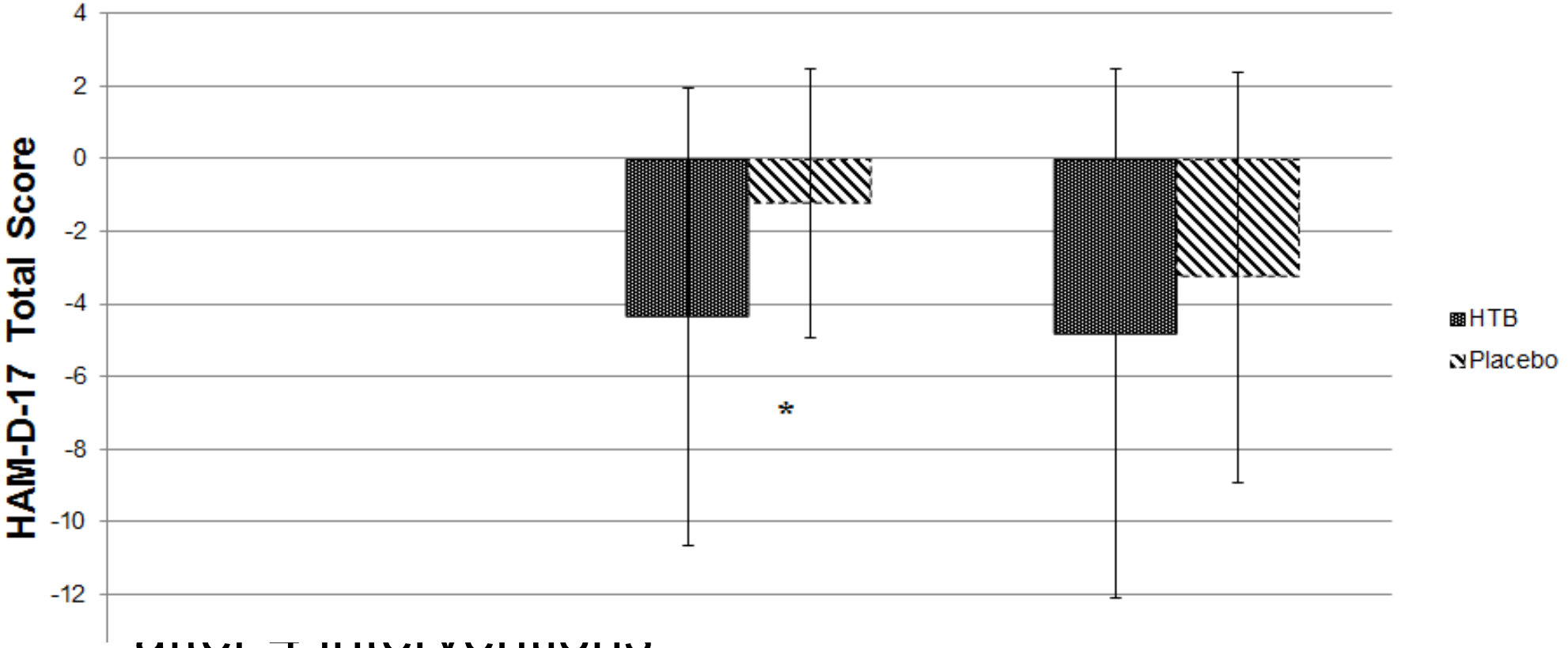
HTB HAM-D$_{\text{total score}}$ ITT analysis

3.14 points difference

(*P* = .031)

1.88 points difference

(*P* = .199)



after 4 interventions

effect size Cohen ***d* = 0.72**

4 weeks after treatment

effect size Cohen ***d* = 0.33**

HTB severity of depression

Greater improvement

- With more severe depression
  - HAM-D > 22 at baseline
    - difference in HAM-D scores of **6.17**
  - HAM-D > 26 at baseline
    - difference in HAM-D scores of **10.8**
- In group with antidepressants

Threshold for clinical significance of the National Institute for Clinical Excellence (NICE):

treatment-placebo difference of **3 points** on the HAM-D

HTB Adverse effects

reported by 21 participants

- 12 (86%) in the HTB group
- 9 (56%) in the control group

No serious adverse events

But: HTB are an important cause of sudden death in Japan,

Temp of hot baths 42°C and more

HTB vs Physical exercise

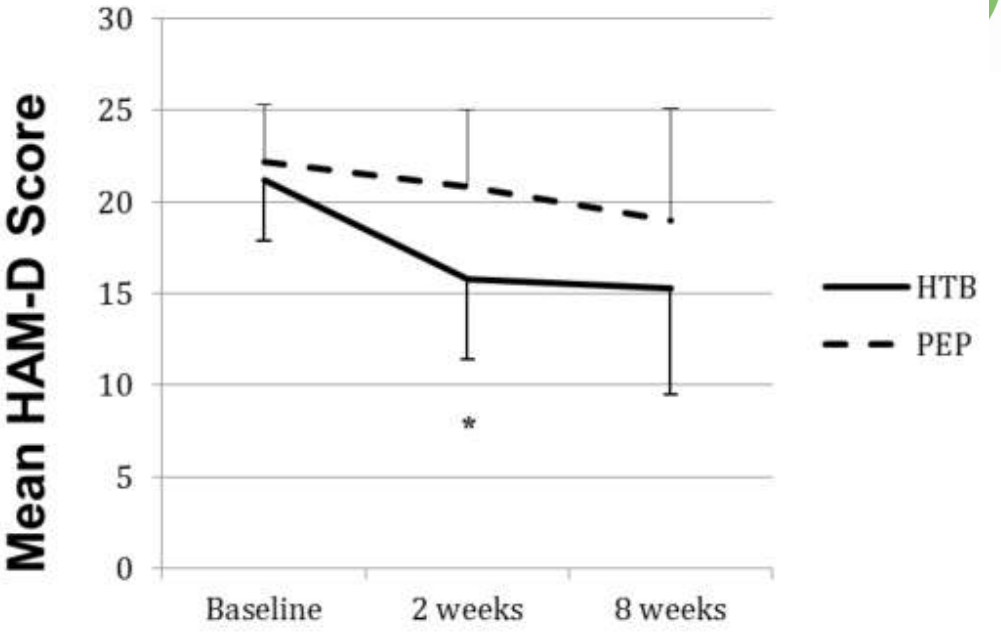
- Pilot study, parallel-group, randomized controlled trial
- 45 depressed patients with Hamilton Scale for Depression (HAM-D) total score **≥ 18** (mean HAM-D 21.7)
  - 22 HTB
  - 23 Physical exercise
    - in groups moderate intensity aerobic exercises

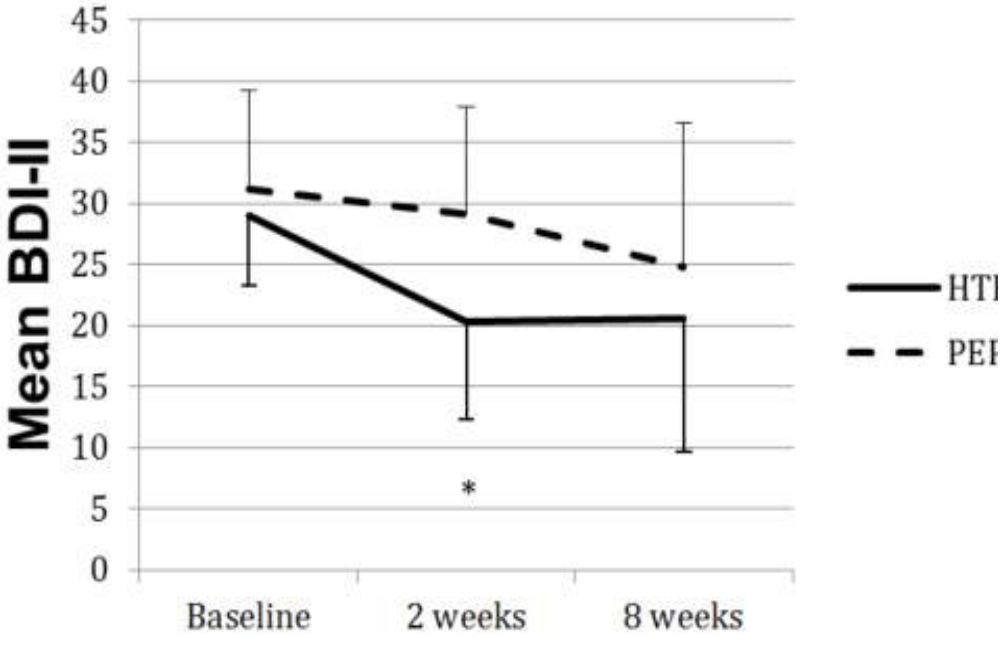
Naumann J, et al. Effects and Feasibility of Hyperthermic Baths for Patients with Depressive Disorder: A Randomized, Controlled Clinical Pilot Trial. (Under peer review in American Journal of Psychiatry)

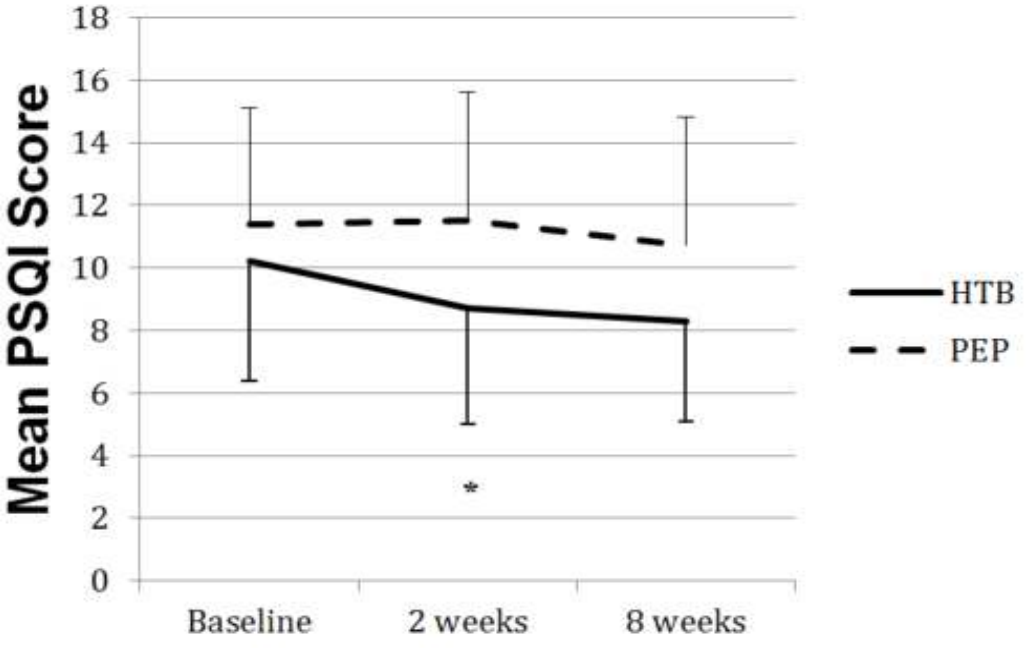
HTB vs Physical exercise

–Sign. and relevant improvement of depression and sleep after 2 weeks (ITT)

- HAM-D 4.3
- BDI 7.5
- PSQI 2.0







Hyperthermia methods

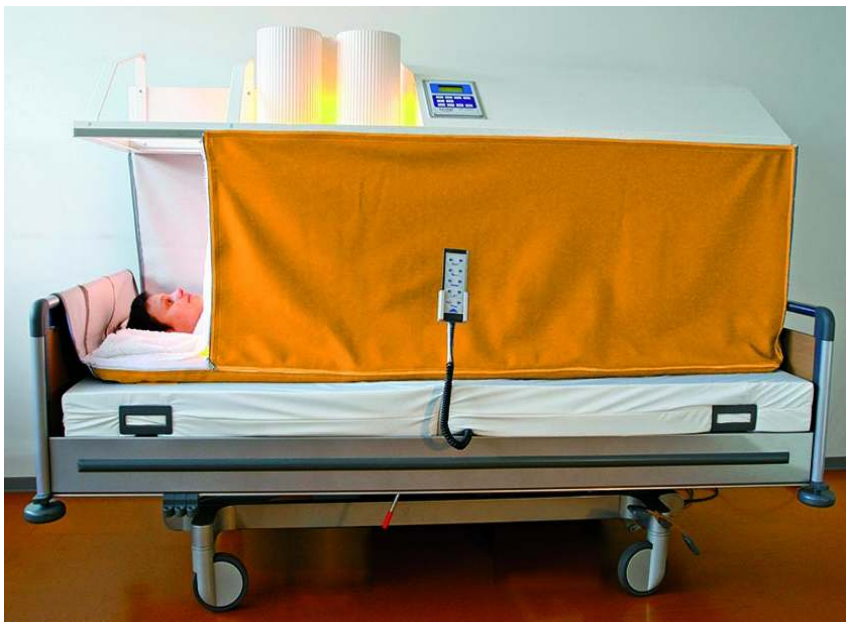
Exogen

- **Hyperthermic Baths**
- **Infrared Light, Sauna**
- Capacitive fields
- Microwaves

Endogen

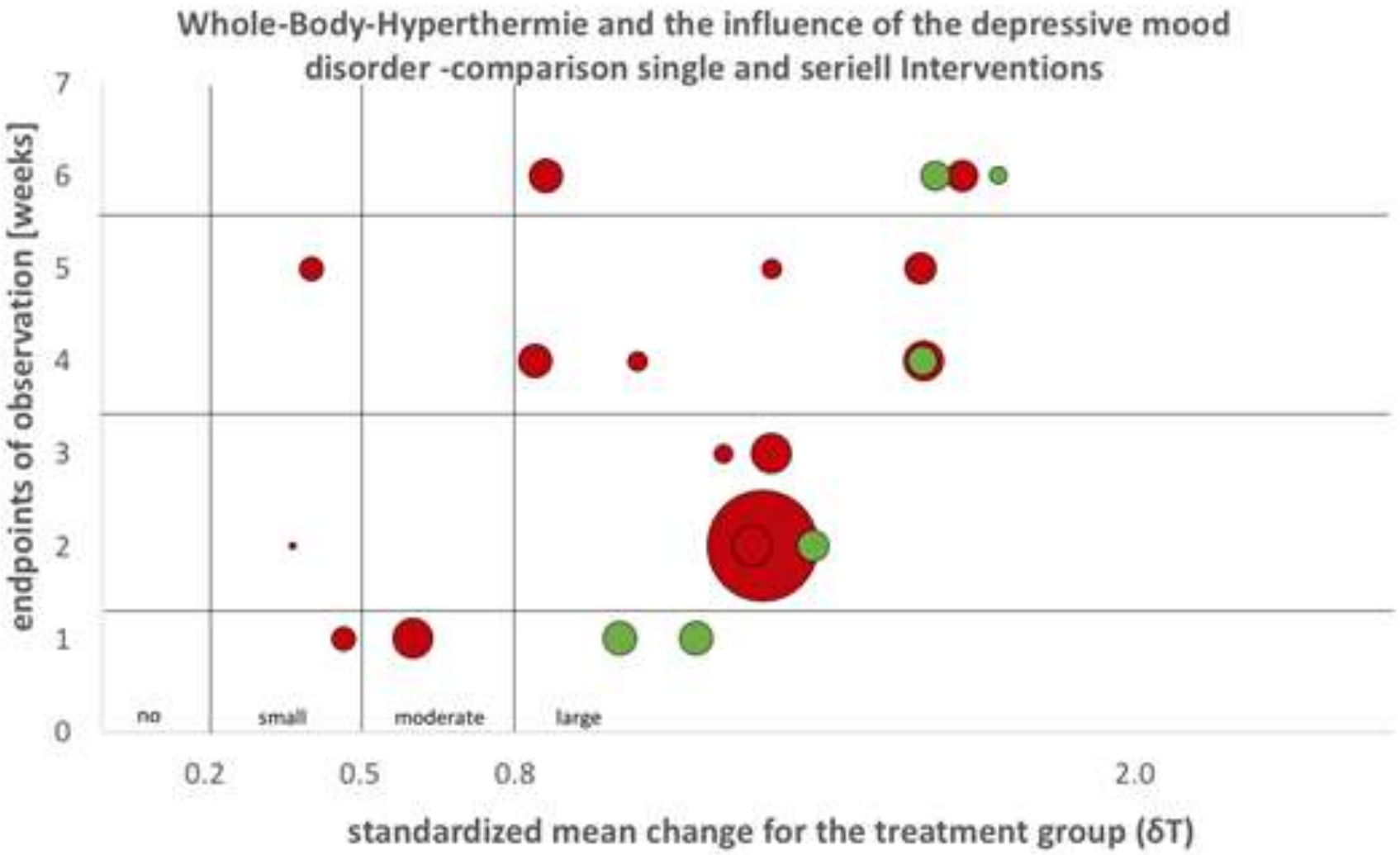
- Misteltoe (Lectins)
- cell extract of gram neg bacteria

Keidel-Bad Freiburg



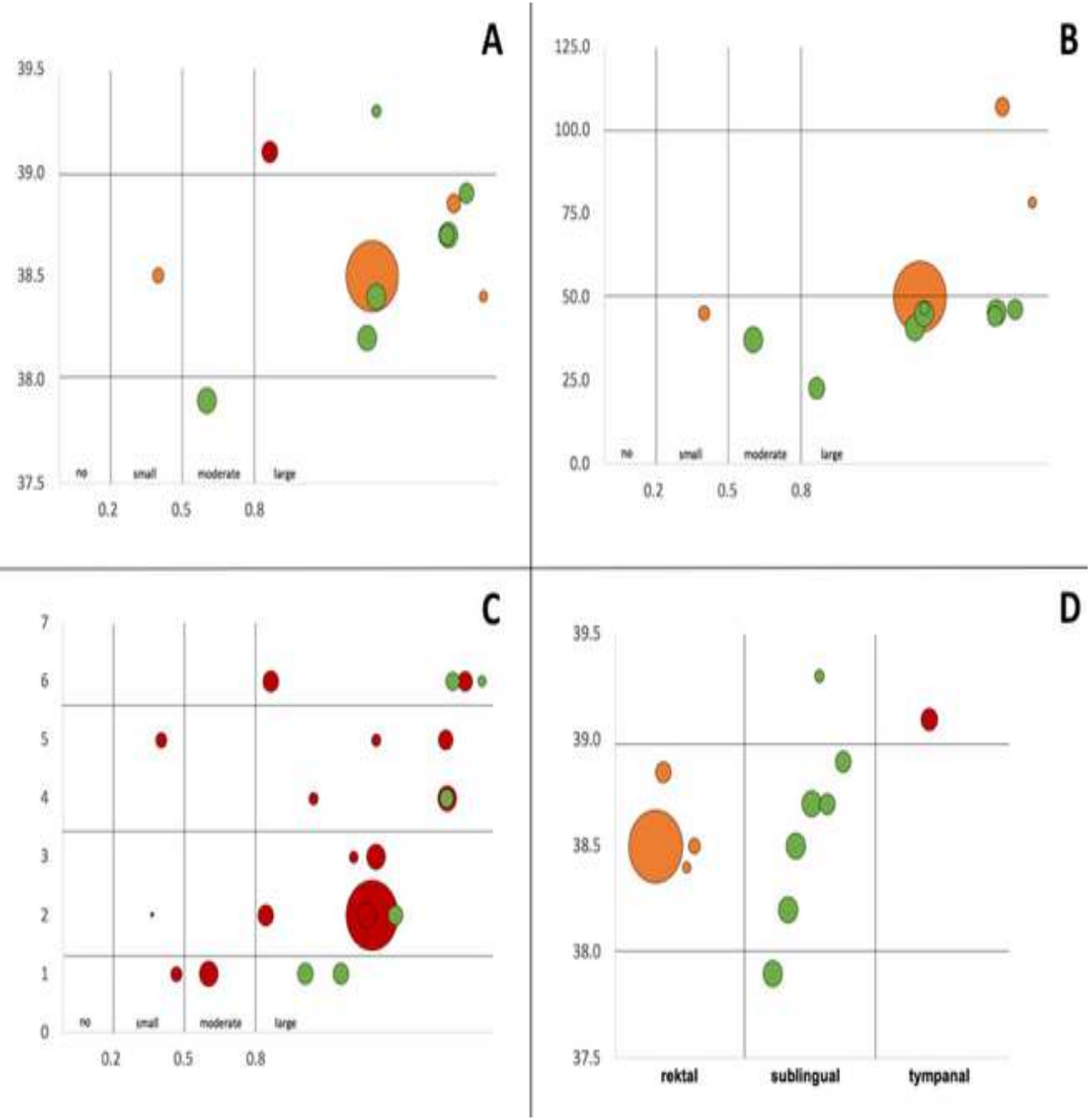
https://www.heckel-hyperthermia.com/index.php/en05#gallery9ddb70d768-1

Correlations of effects and methods



Red= seriell intervention

Correlations of effects and methods



Correlations of effect and

- **A**:max. body core temperature
  - Orange=rectal;
  - green=sublingual
  - red=tympanic
- **B**: treatment time (minutes)
  - Orange=infrared light
  - Green=baths
- **C**: Endpoint (weeks)
  - Red= serial
  - Green=single intervention
- **D**: max. body core temperature and method to measure

K.U.Hanusch, published soon

Finish Sauna longterm effects

2000 people observed for 20 years

Sauna visits per week	1x	2-3x	4-7x
Risk for			
•Sudden cardiac death	10%	8%	5%
•Mortality by CVD	22%	16%	12%
•Overall mortality	49%	38%	31%

= Risk reduction with frequent sauna

40-50% to die

60% for stroke

35-40% for respiratory diseases

50% cancer

50% dementia

Laukkanen T, Khan H, Zaccardi F, Laukkanen JA. Association Between **Sauna** Bathing and Fatal Cardiovascular and All-Cause Mortality Events.JAMA Intern Med. 2015 Feb 23.

Hyperthermia in depression
Conclusions

- May have a relevant effect (larger trials needed)
- Larger effects in severe depression
- Fast onset of treatment effects (IR-HT even immediate)
- Less adverse effects than many antidepressants
- HTB more helpful with antidepressant medication
- IR-HT larger and longer lasting effects

Many open questions:

- HTB or IR-WBH
- Single or seriell intervention
- Max. body core temperature …

Aquafitness-
The new trend in Balneotherapy

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Exercise on land

Exerise is very healthy

But weight is distress for joints and spine

Ideal training consists of strengthening exercises without distress

Aquafitness provides these aspects

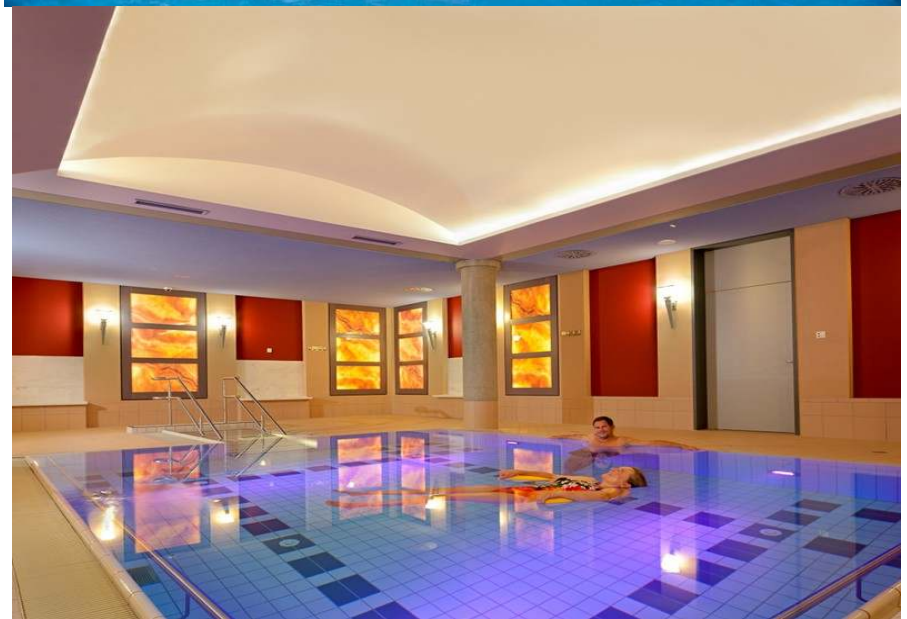
https://www.lifeline.de/galerien/

Training of mobility

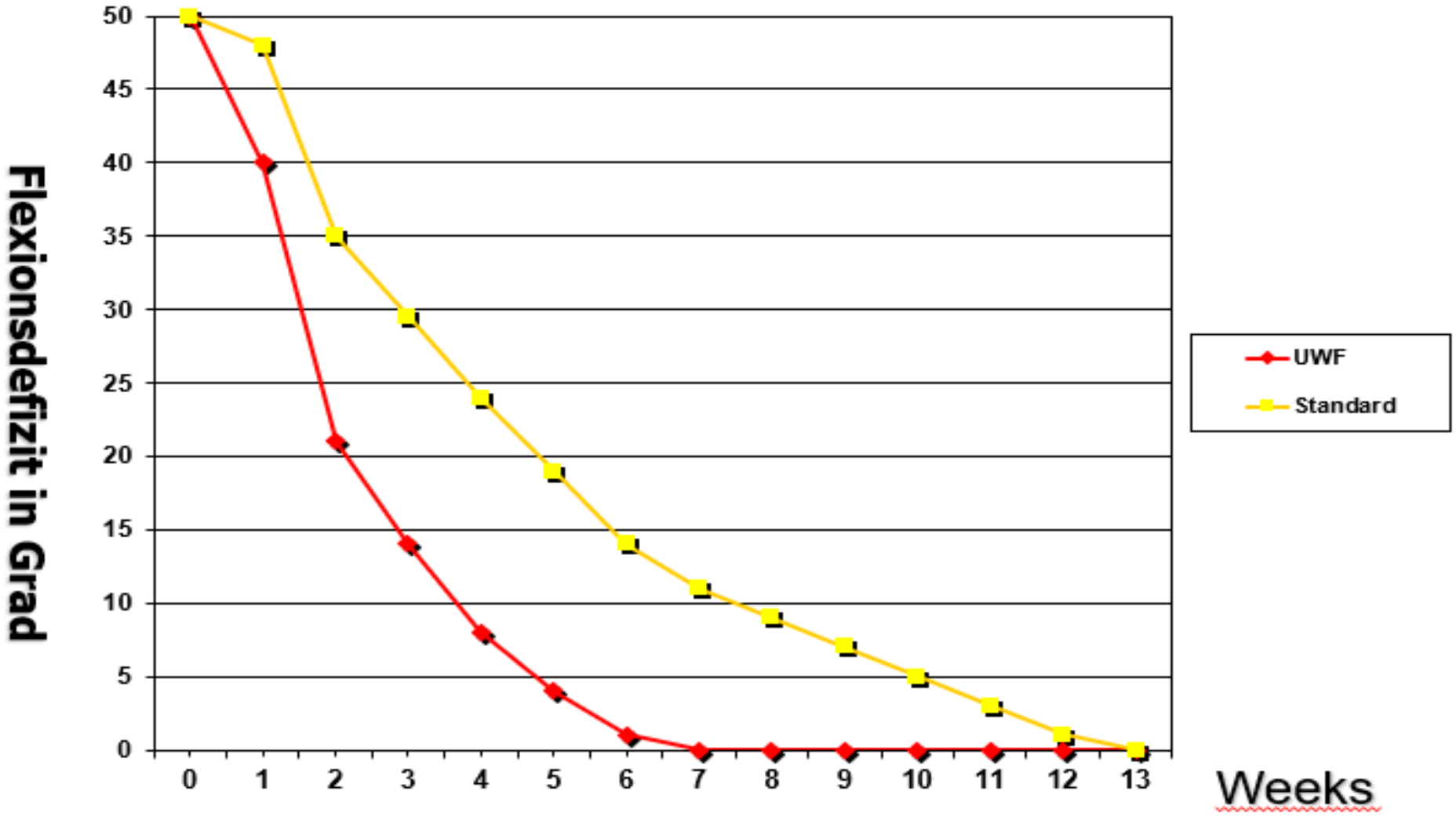
Most important
- Relief through floating
- Relaxation do to thermoneutral or warm water
- Slow movements

- In acute conditions
- Direct after operations
- Elder people

Foto: Touristeninfo Badenweiler



Mobility of the knee after operation



Yellow Land Red water cycle

Gymnastic groups every day

Uhrzeit | Tag	Montag	Dienstag	Mittwoch	Donnerstag	Freitag	Samstag	Sonntag
09.30 - 09.50 Uhr	◪			◪			
10.00 - 10.20 Uhr	◪	◪	◪	◪	◪	◪	
10.30 - 10.50 Uhr	◪	◪	◪	◪	◪	◪	
11.00 - 11.20 Uhr	◪	◪	◪	◪	◪	◪	
11.30 - 11.50 Uhr	◪	◪	◪	◪	◪	◪	
14.30 - 14.50 Uhr	◪	◪	◪	◪	◪		
15.00 - 15.20 Uhr	◪	◪	◪	◪	◪		
15.30 - 15.50 Uhr	◪	◪	◪	◪	◪		
16.00 - 16.20 Uhr	◪	◪	◪	◪	◪		
16.30 - 16.50 Uhr	◪	◪	◪	◪	◪		
17.00 - 17.20 Uhr		◪	◪	◪	◪		
19.00 - 19.20 Uhr		◪	◪		◪		
19.30 - 19.50 Uhr		◪	◪		◪		

Training of strength

Also Water resistance important

Great variety of intensity

- Aerobic
  - Aquafitness
- Anaerobic
  - Aqua-Drill
- Resistance training for muscles
- With or without contact to floor
  - Aqua-Jogging

Devices

Enlarging surface

Larger devices
- Aqua-Cycling
- Aqua-Jumper

Additional motivation (music)
- Aqua-Zumba

Aquafitness and overweight

- No weight in the water
  - Relieves strain on joints
- Water pressure
  - Improves respiration
  - More blood back to the heart
- Better cooling
  - Even in water up to 34°C
  - Enables more intense training
- Less appetite after Aquafitness in thermoneutral water
- Improves blood cholesterol

Aquafitness in overweight own study

84 healthy participants, all overweight BMI > 25 kg/m²

3 groups, Exercise 20 times in 12 weeks

- Aquafitness
- Exercise in fitness center
- Exercise at home

Aquafitness and fitness center better than exercise at home in

- Fitness-test; 6-minutes-run-test
- loss of weight about 5kg
- quality of life

Less problems with Aquafitness

Aquafitness in overweight with knee problems

87 overweight participants with knee problems

2 groups

- Aquafitness
- Exercise at home

Less weight 10kg in 6 months

Less pain in VAS 6,5 to 4,1

No improvement in group with exercise at home

Aquafitness for elderly

- Floating in the water
  - Lower risk of falls
  - Vertigo improves
- Water resistance
  - Mild training
  - Resistance adaptable anytime
  - Training with younger people easy
- Warm water
  - Relaxation of muscles
- Water pressure
  - Improves reflux of the blood
  - Good for hypertension

Forests, Shinrin-yoku and their importance for Health (Spa) resorts

Foto Eva Kempinger http://www.waldkurort.de/

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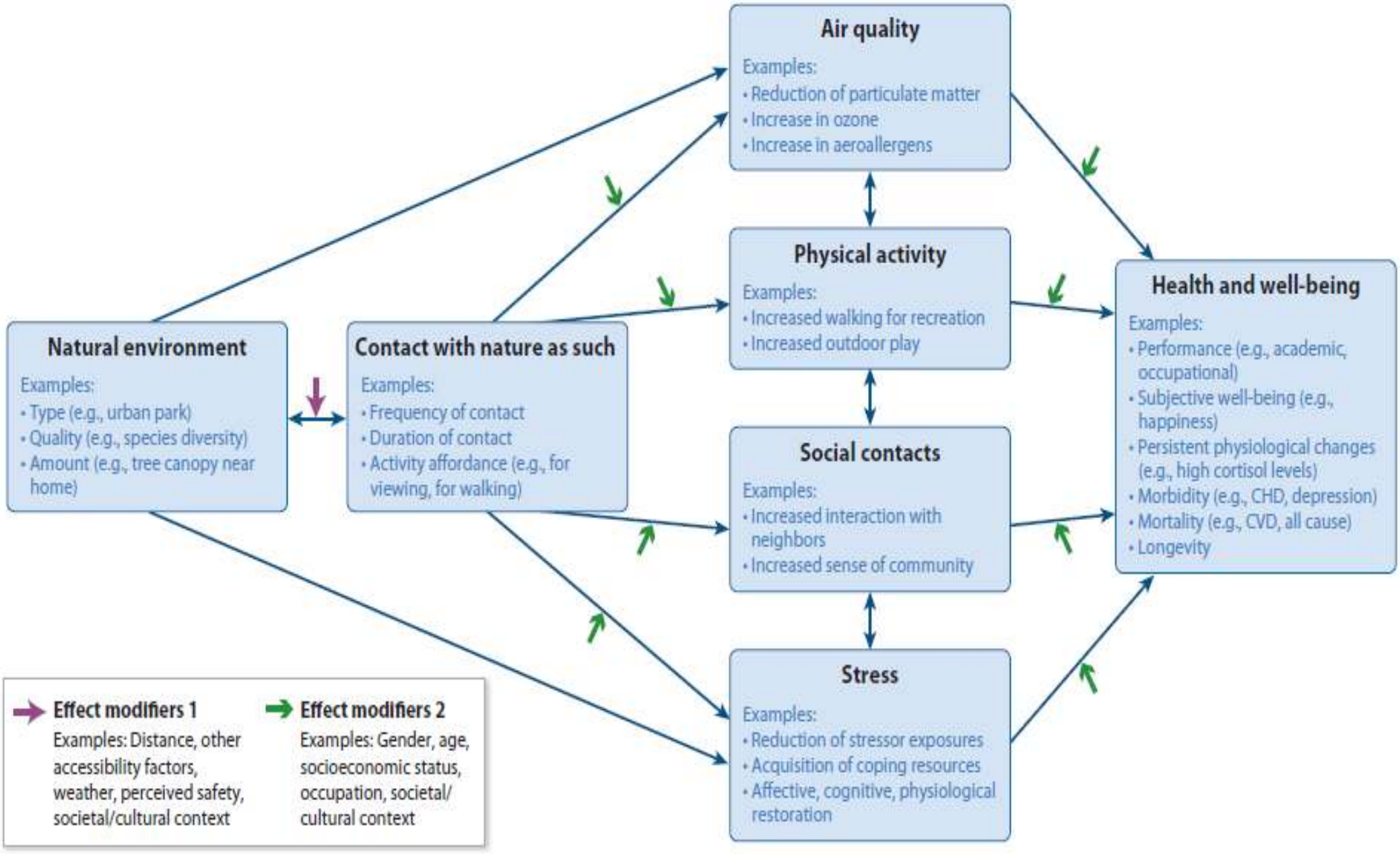
Pathways through which contact with Nature relates to Health



Pathways through which contact with Nature relates to Health

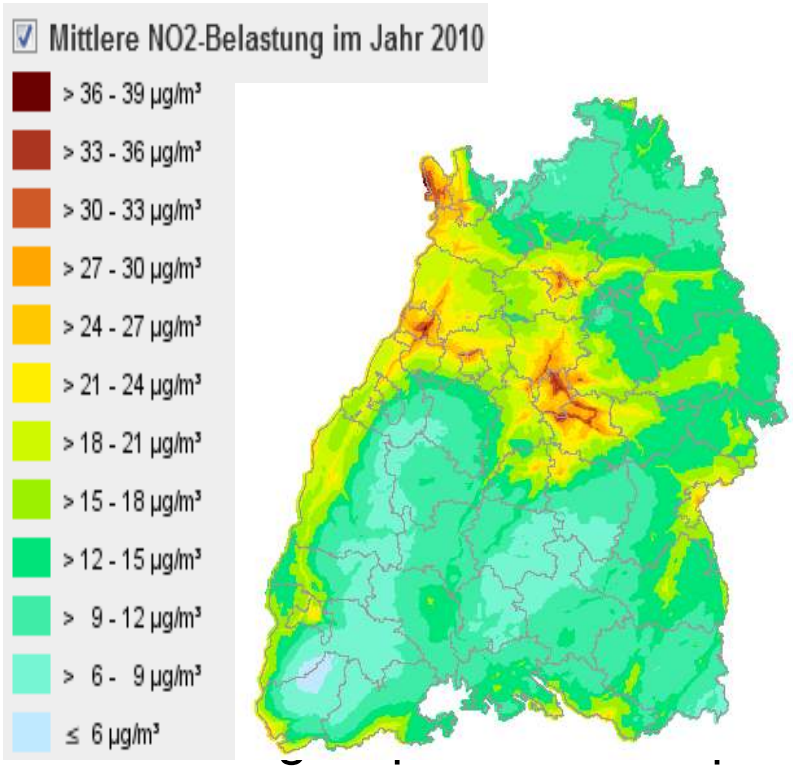
Air Quality

- Trees reduce levels of air pollutants [e.g., ozone, oxides nitrogen (NOx), oxides of sulfur] and PM
- reduce air movement

Table 4.2 Potential effects of forests on deposition fluxes

		Moorland	Forest	% increase forest/moor
Canopy height	h (m)	0.15	10	–
Zero plane displacement	d (m)	0.1	7	–
Roughness length	z_o (m)	0.01	1.0	–
Friction velocity	$u*$ (m s^{-1})	0.32	0.82	156
Momentum flux	ϑ (N $m^{-2)}$	131	840	541
Maximum deposition velocity for SO_2	V_{max} SO_2 (mm s^{-1})	18.6	35.1	89
Maximum deposition velocity for NO_2	V_{max} NO_2 (mm s^{-1})	20.0	43.5	118
Maximum deposition velocity for NH_3	V_{max} NH_3 (mm s^{-1})	21.4	55.5	160

Air Quality, Forrest (Schwarzwald)



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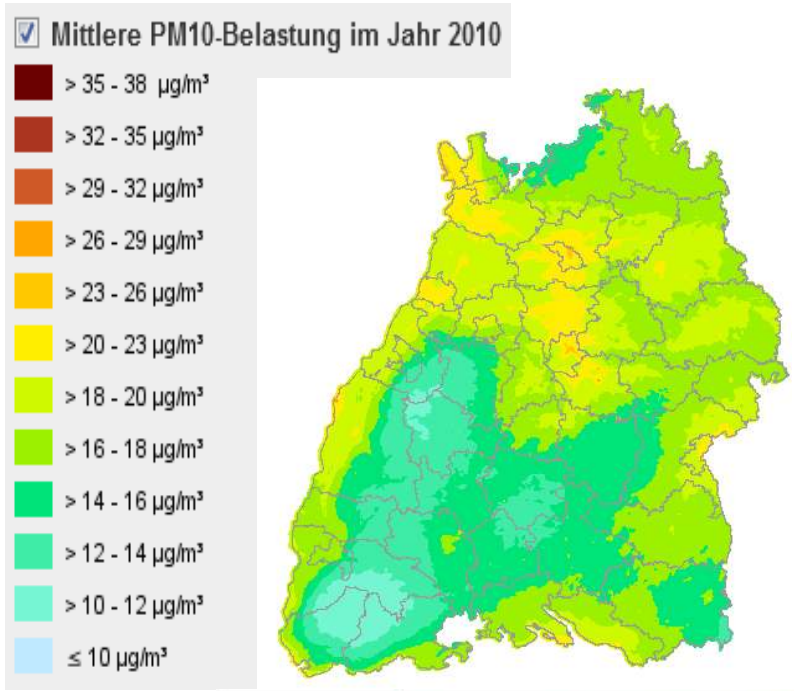
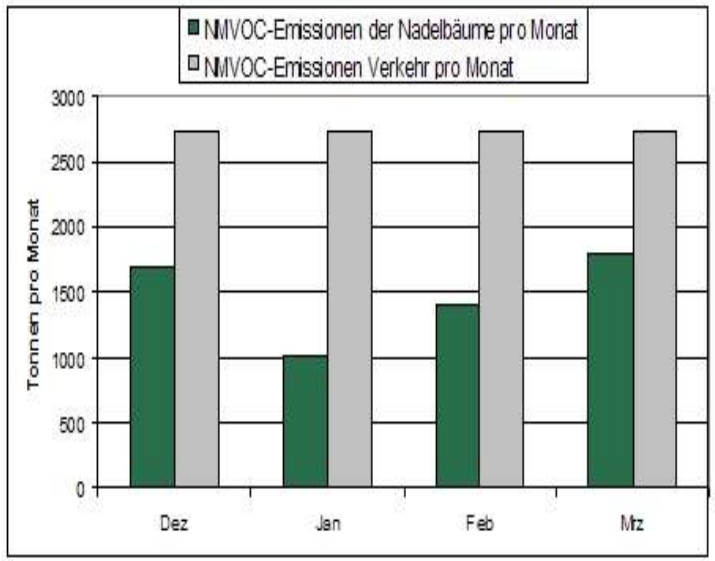




Grafik: Typische NMVOC-Emissionen in den Monaten von Dezember bis März in Baden-Württemberg.
Quelle: LUBW

Physical Activity

promotes physical and mental health across the life span

Association of NE and physical activity

- Children: positive in 40% of the studies
- Older people: positive in 7 out of 8 studies
- health benefits largest among the laziest

Important

- individuals'(perceived) safety
- accessibility

*Hartig et al.*Annu. Rev. Public Health 2014.35:207

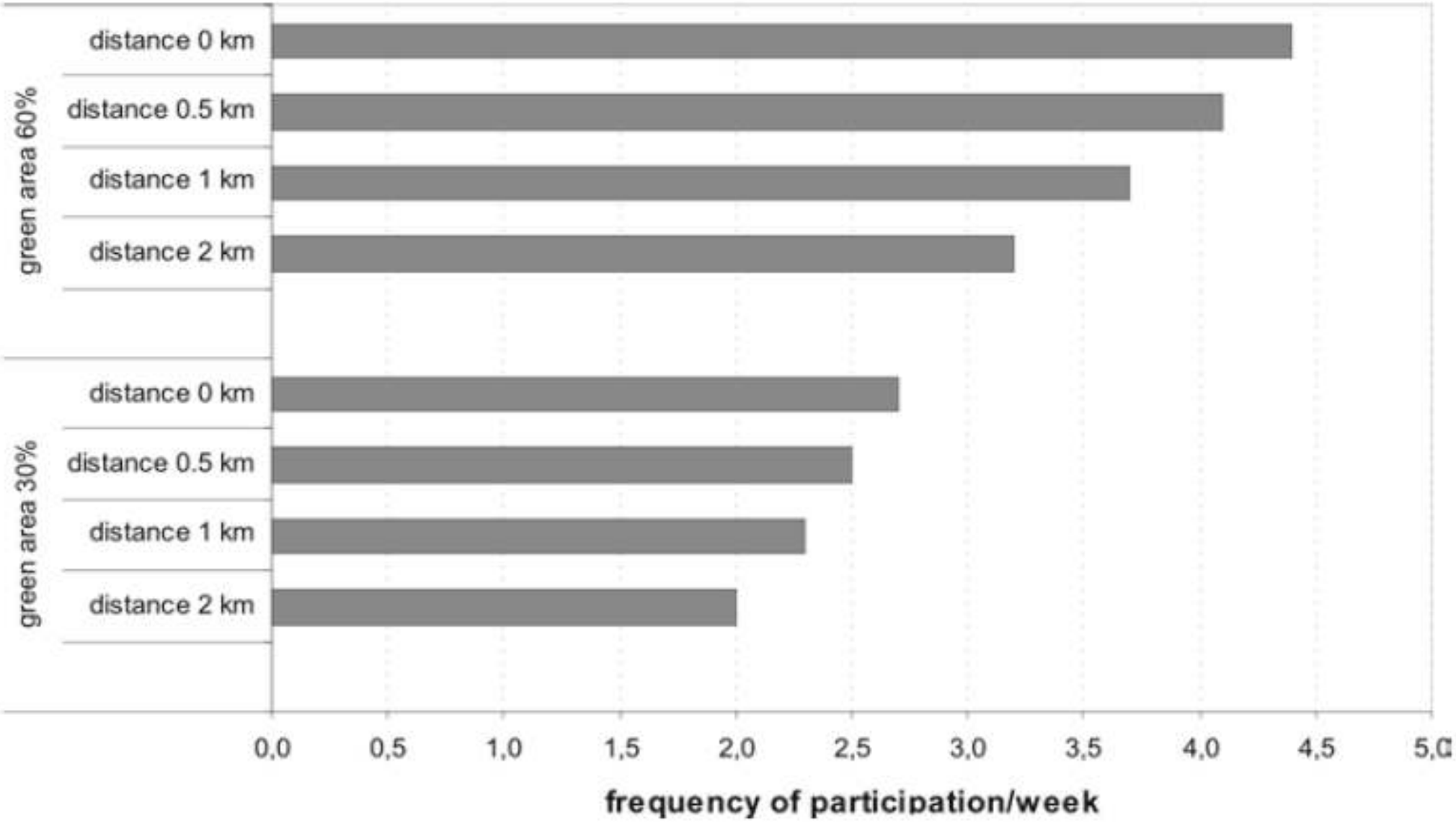


Fig. 9.1 Estimated frequency of participation in close-to-home outdoor recreation per week in two different recreation opportunity situations, with 30% respectively 60% of the total neighborhood area consisting of green space (Neuvonen et al. 2007)

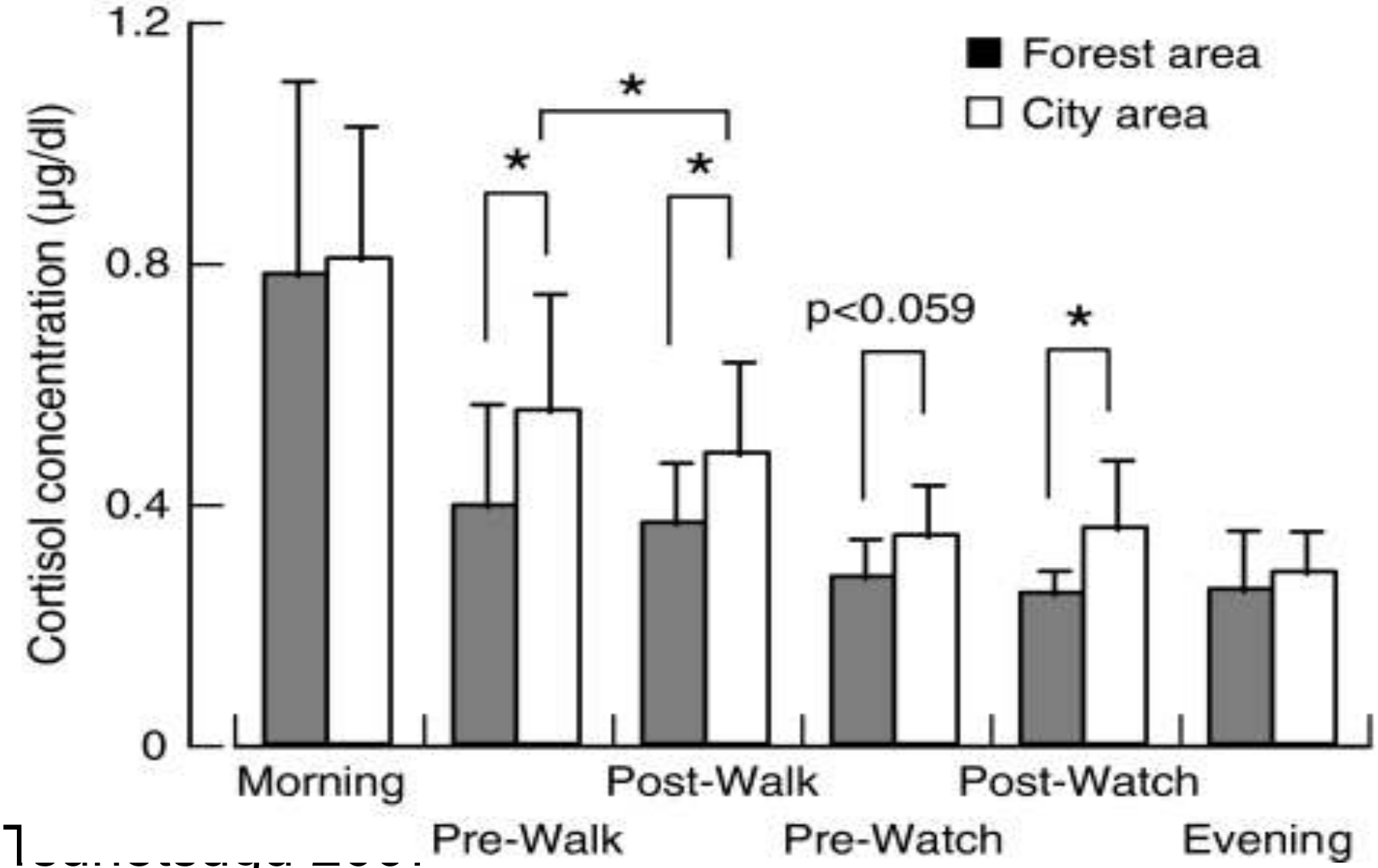
Social Cohesion

positive association between social relationships and health and well-being

association between social cohesion and

- greenness of the neighborhood Sugiyama et al
- quantity and even stronger quality of greenery. De Vries et al

Stress reduction Influence on Cortisol



Blood presssure and distress (Qing Li u. a. 2011).

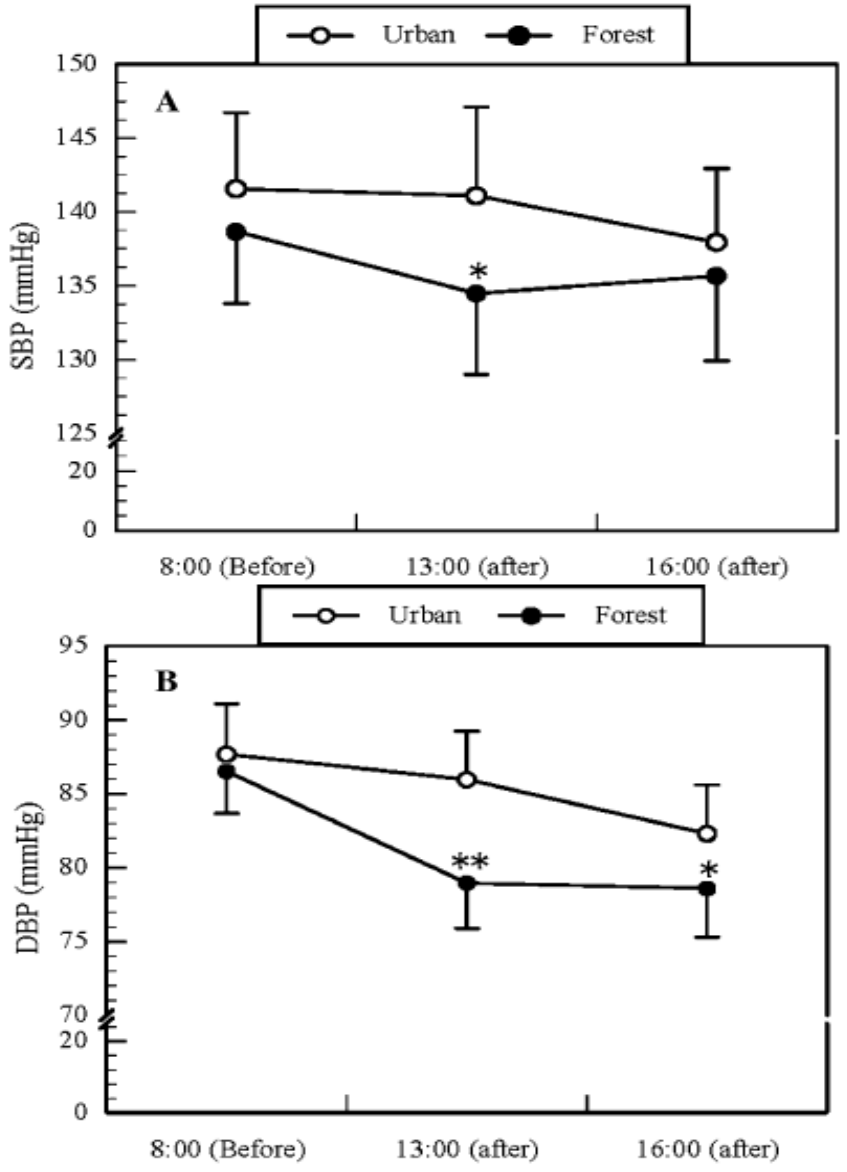


Fig. 2 Effect of walking in a forest park and walking in an urban area on the levels of systolic (**a**) and diastolic (**b**) blood pressure. Data are presented as the mean + SE ($n = 16$). $^{*}p < 0.05$, $^{**}p < 0.01$, significantly different between the forest and urban trips according to the paired t test

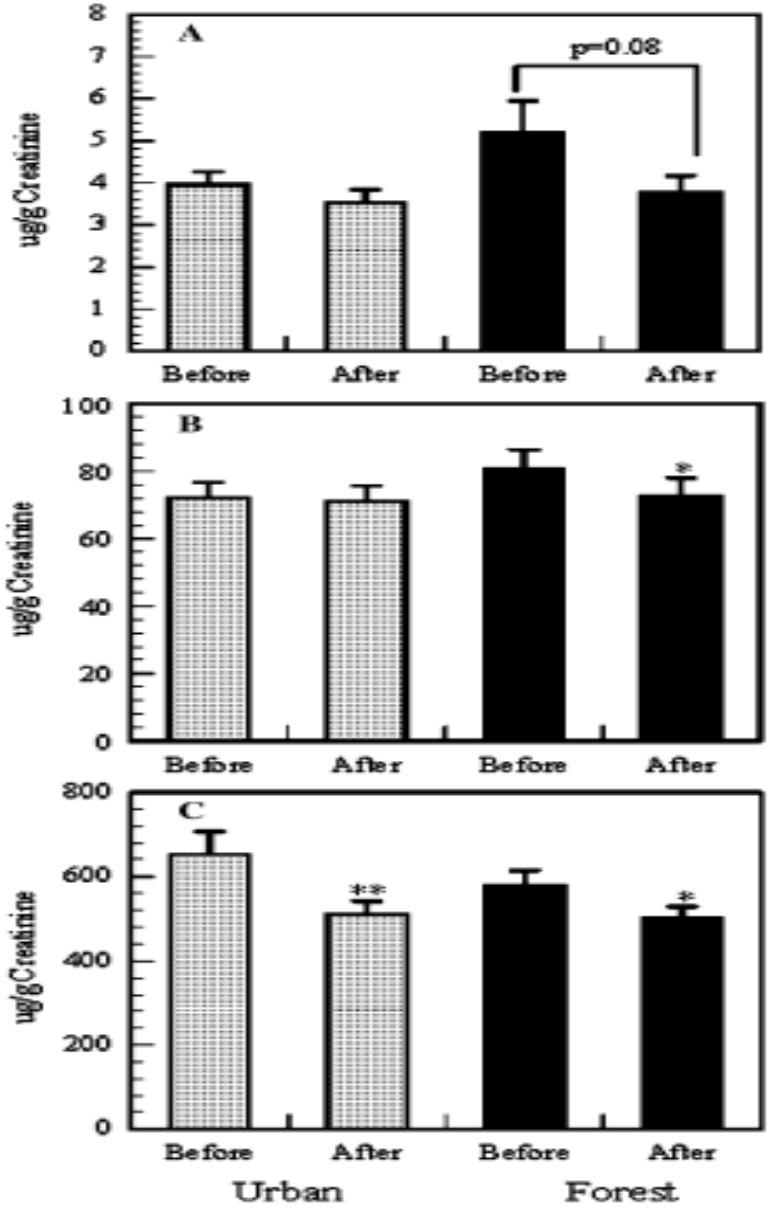
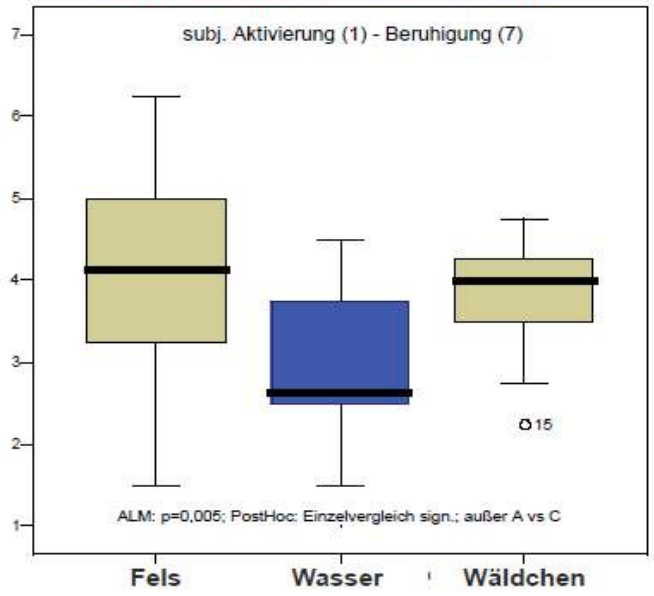


Fig. 3 Effect of walking in a forest park and walking in an urban area on urinary adrenaline (**a**), noradrenaline (**b**), and dopamine concentrations (**c**). Data are presented as the mean + SE ($n = 16$ for adrenaline and $n = 14$ for noradrenaline and dopamine). $^{*}p < 0.05$, $^{**}p < 0.01$, significantly different between after and before according to the paired t test

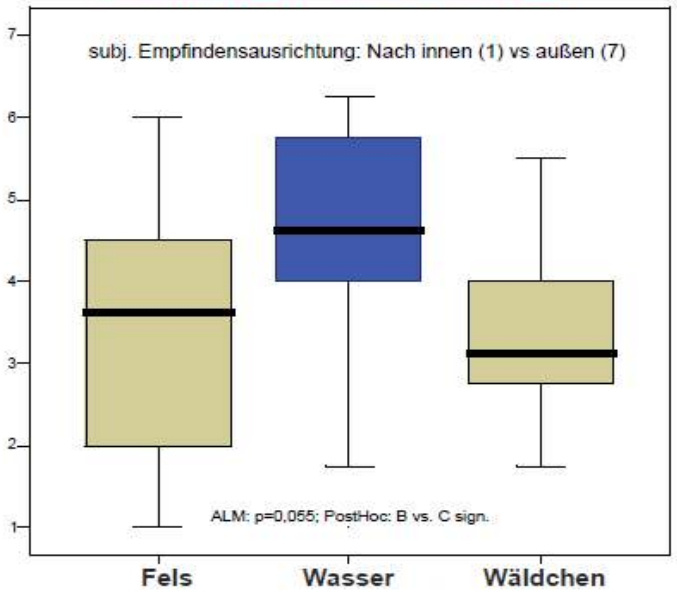
Effects of different NE

Ergebnisse / Basler Befindlichkeitsskala

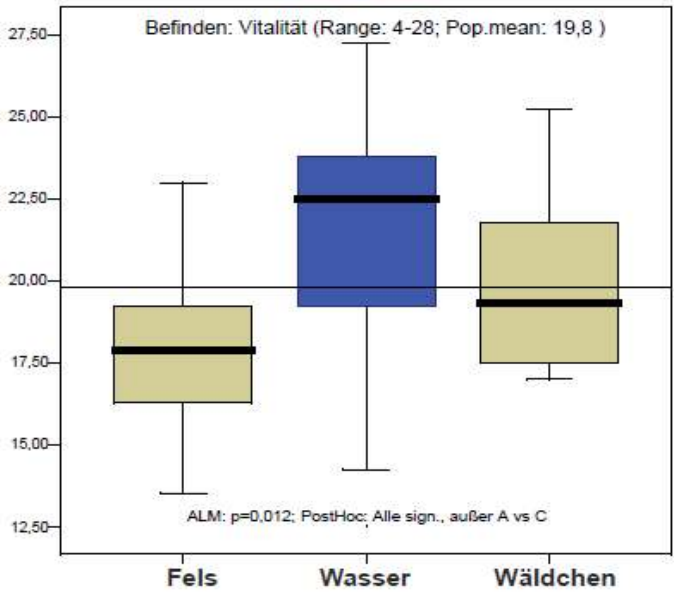
AKTIVIERUNG – BERUHIGUNG



NACH INNEN – NACH AUSSEN



VITALITÄT



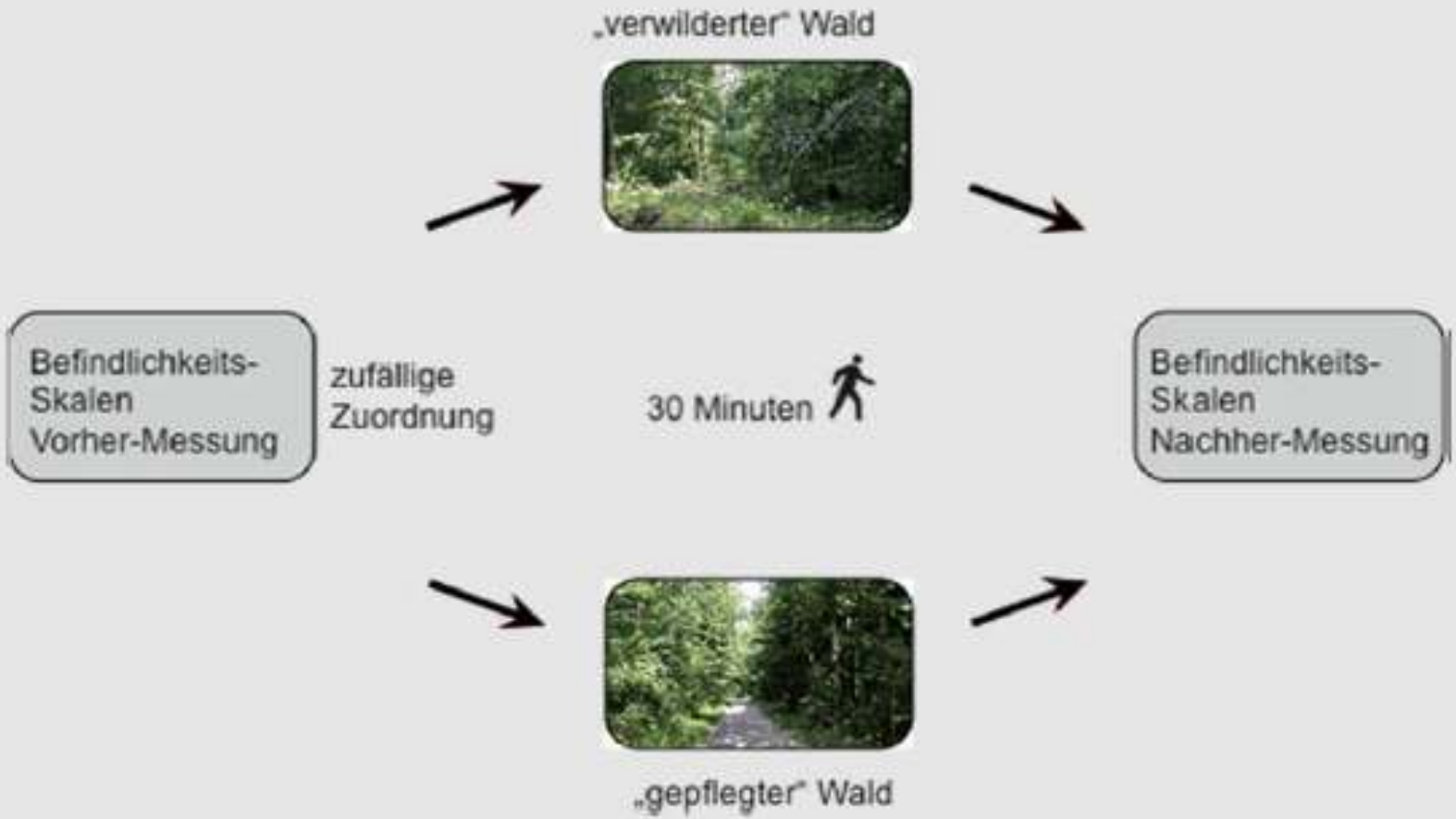
Stein

Wasser

Wäldchen

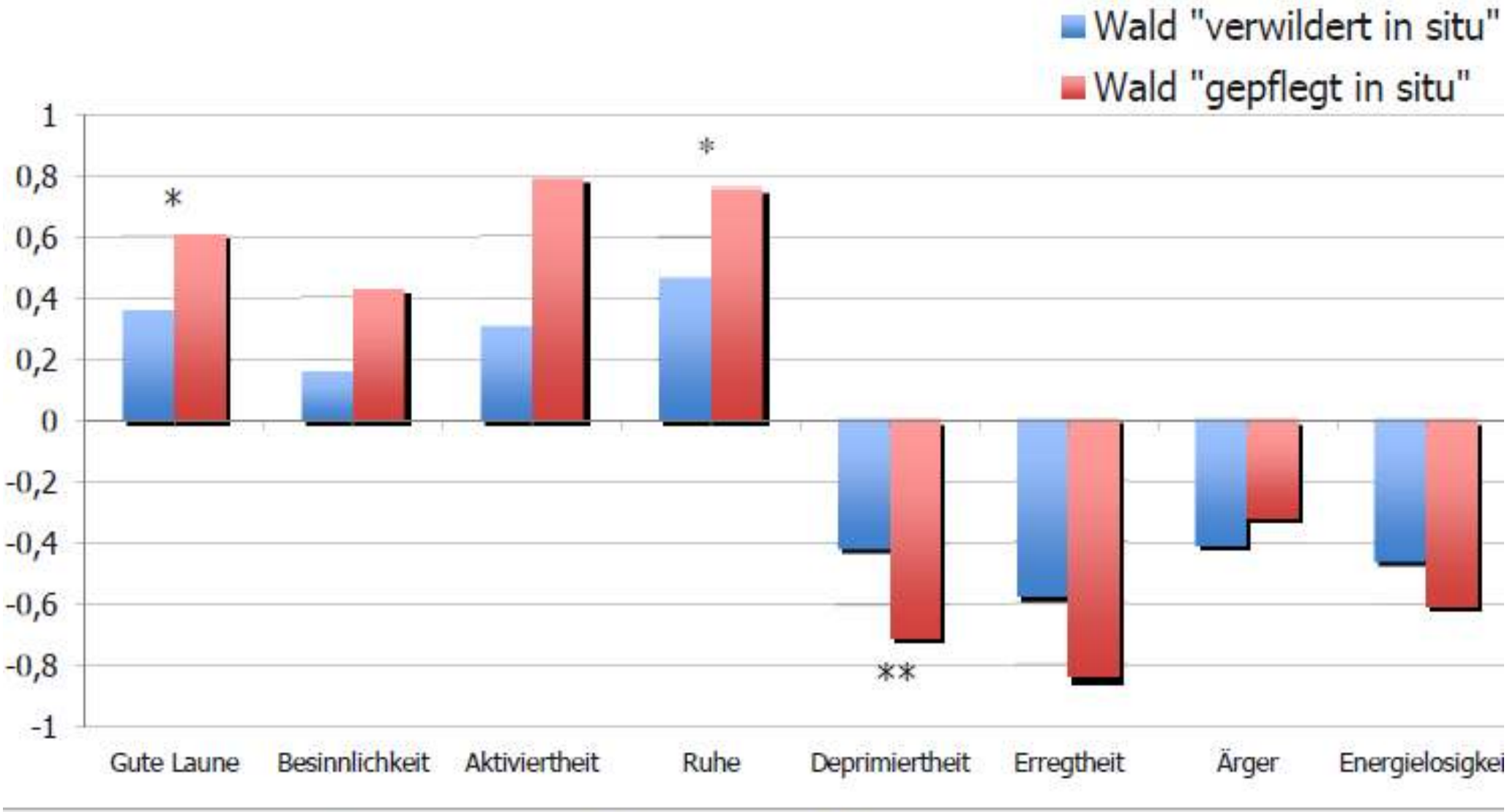
Wild or cultivated forest

Design experimentelle Studie 1: in situ



Wild or cultivated forest

Vergleich zwischen Bedingungen



Kovarianzanalyse, Kovariate t1, Abhängige Variable t2-t1; Irrtumswahrscheinlichkeiten:* p<.05, ** p<.01, *** p<.001.

Forests in therapy

- Erholungswald recreation forest
  - For all people, clean air
- Kurwald „health forest“
  - Also ill people, secondary prevention, therapeutic walking, adequate infrastructure
- Heilwald „healing forest“
  - Mainly therapeutic use, accessable onlly for the target group (patients), more special onfrastructure

Conclusion

- The scientific literature relating to the effects of shinrin-yoku is still limited.
- Forests have a positive influence on health and wellbeing of people living close to it.
- They have also a positive effect on health and wellbeing, if these places are visited for a certain even short time.
- Even artificial substitutes for forests show positive effects.

- Health resorts mainly situated in natural environments and forests can use the environment as helpful tools to achieve more physical activity and stress reduction in the general population and patients, esp. with chronic diseases related to lifestyle

Medical spa treatment in Baden-Württemberg, Germany: A survey of spa physicians 2016

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Health Resorts (HR) in Germany

Balneotherapy (onsen) is applied in villages comitted to the health = Health Resorts

Certified and controlled by the government (special laws)

Qualities of HR

- Clean air, no noise, little traffic, nature
- Culture, music, parks, hotels, healthy food, …
- Medical institutions and staff
- Physical therapies, Physiotherapy, Sauna, Inhalation,

Balneotherapy in Health resorts

Balneotherapy uses local natural healing remedies

- Thermal mineral water
- Gases: CO_2 , radon, sulphure
- Mud (peloids)
  - organic
  - anorganic (vulcanic stone powder with water)
- Climate

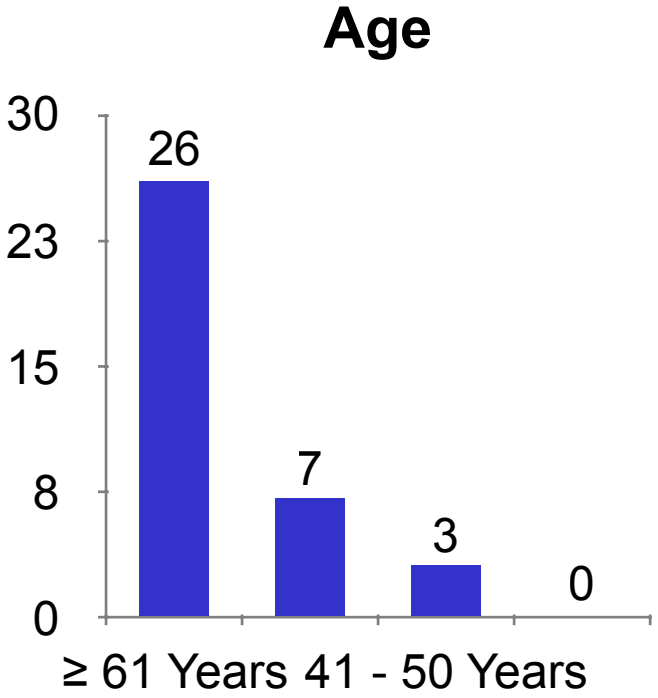
Survey of Balneotherapy in Baden-Württemberg

- 56 Health resorts
- 156 Health resort physicians

Questionnaire to all physicians

Interview per telephone with at least 1 Health resort physician per Health resort, possibly all.

Health resort Physicians (n=56)



state, that health resort medicine can relevantly contribute to solve big health problems as chronic pain, elder patients, overweight

but it is necessary to show the possible benefits to insurances, other physicians and patients.

Indications in HR

- Musculoscelettal system (back pain, osteoarthrosis)
- Relatives of patietns visiting rehabilitaion clinics
- Overweight
- Respiratory disases, allergies

Outcome in HR

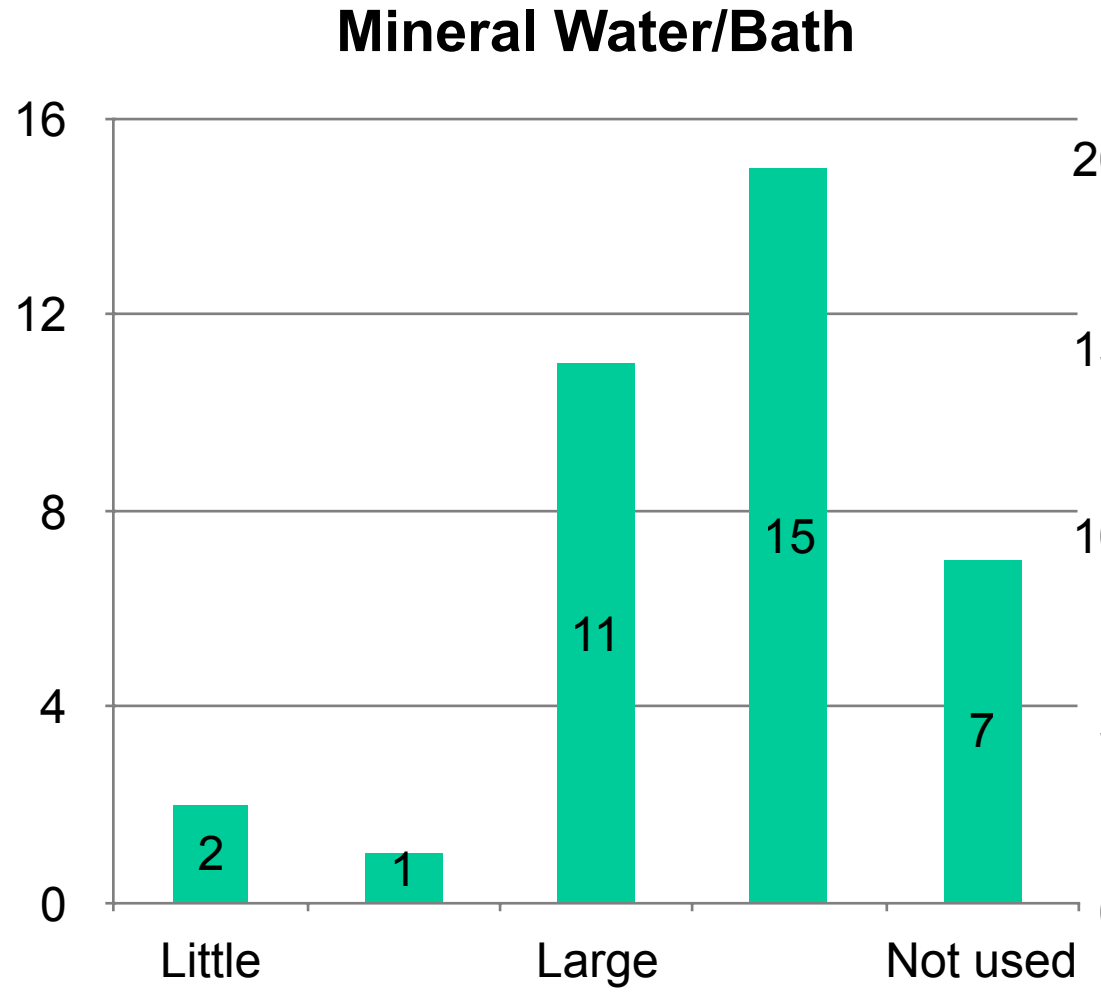
Outcome of patients excellent

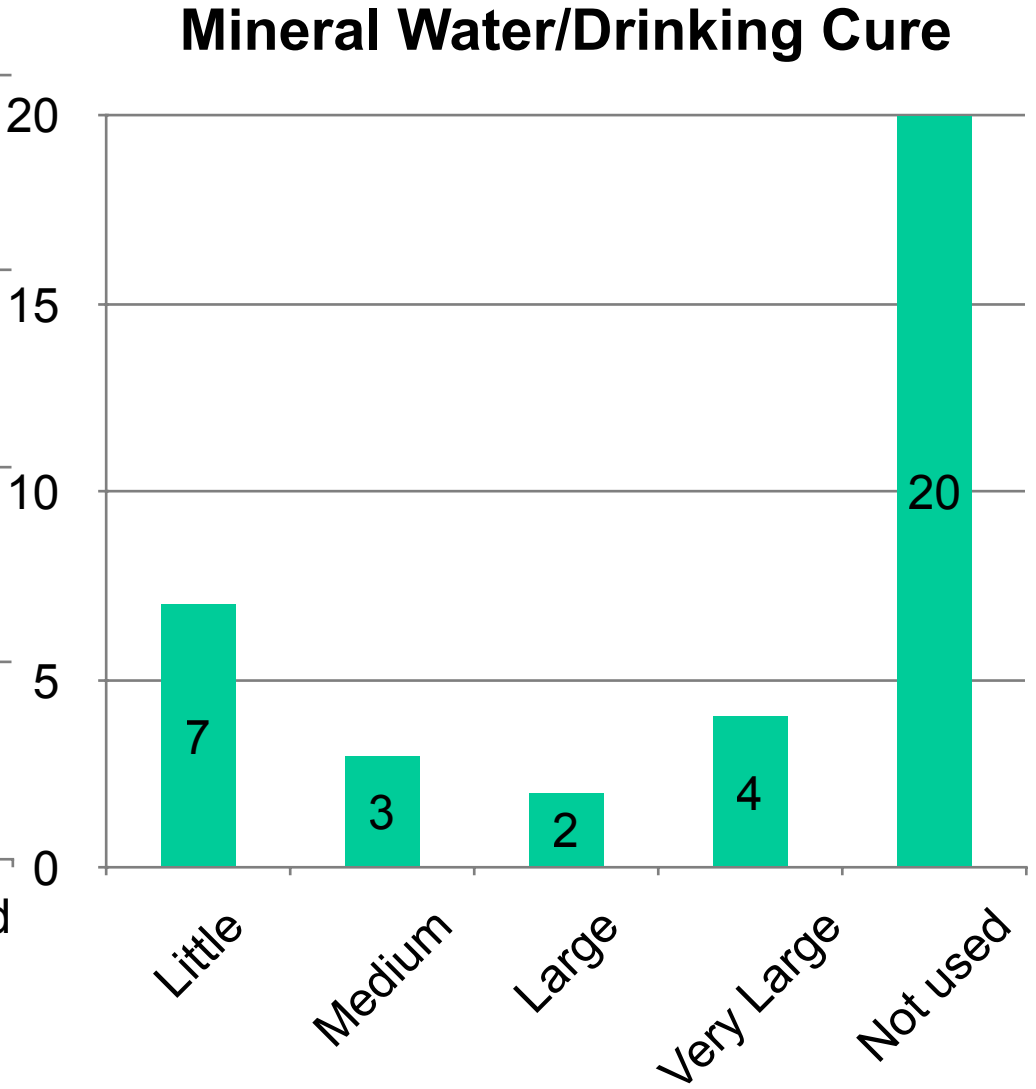
Relevant amelioration in 70 - >90% for nearly all indications

Esp. Musculoscelettal system

Effectiveness of natural remedies

Judged by Health resort physicians





Effectiveness of natural remedies

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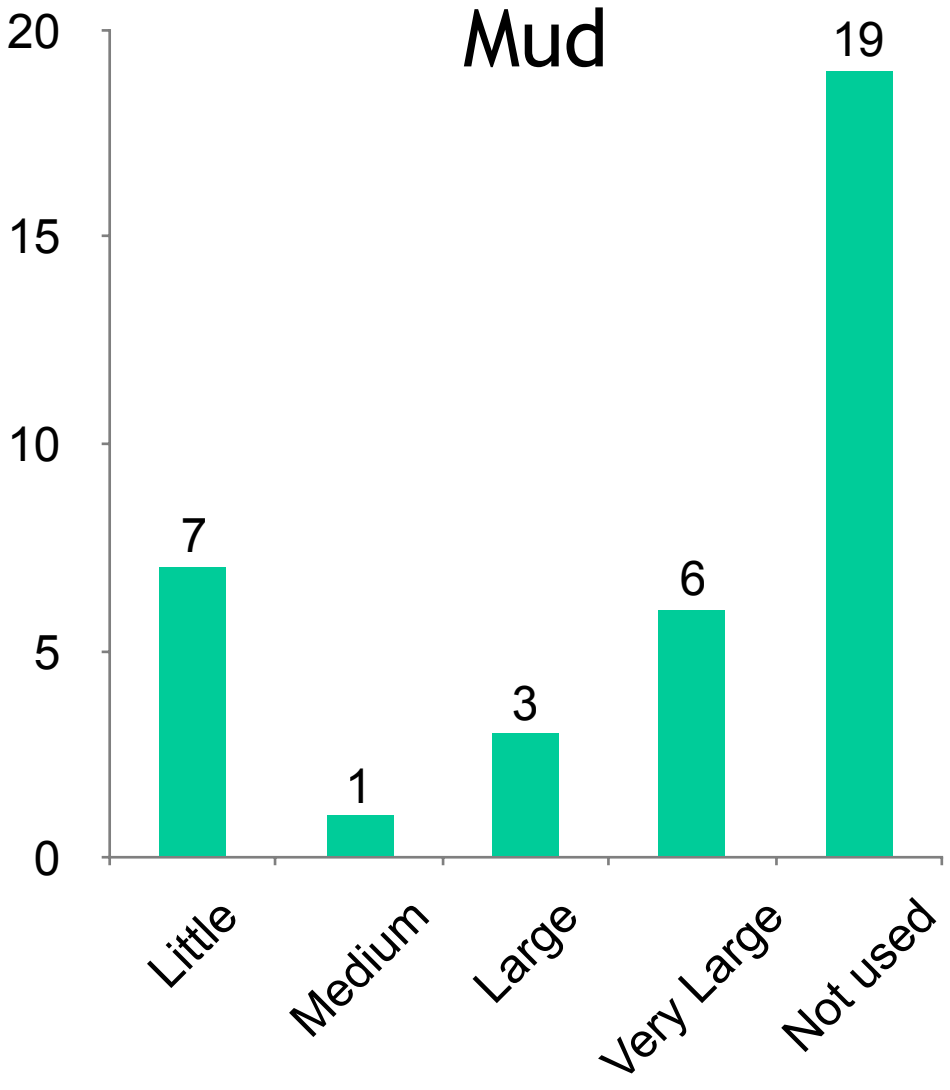
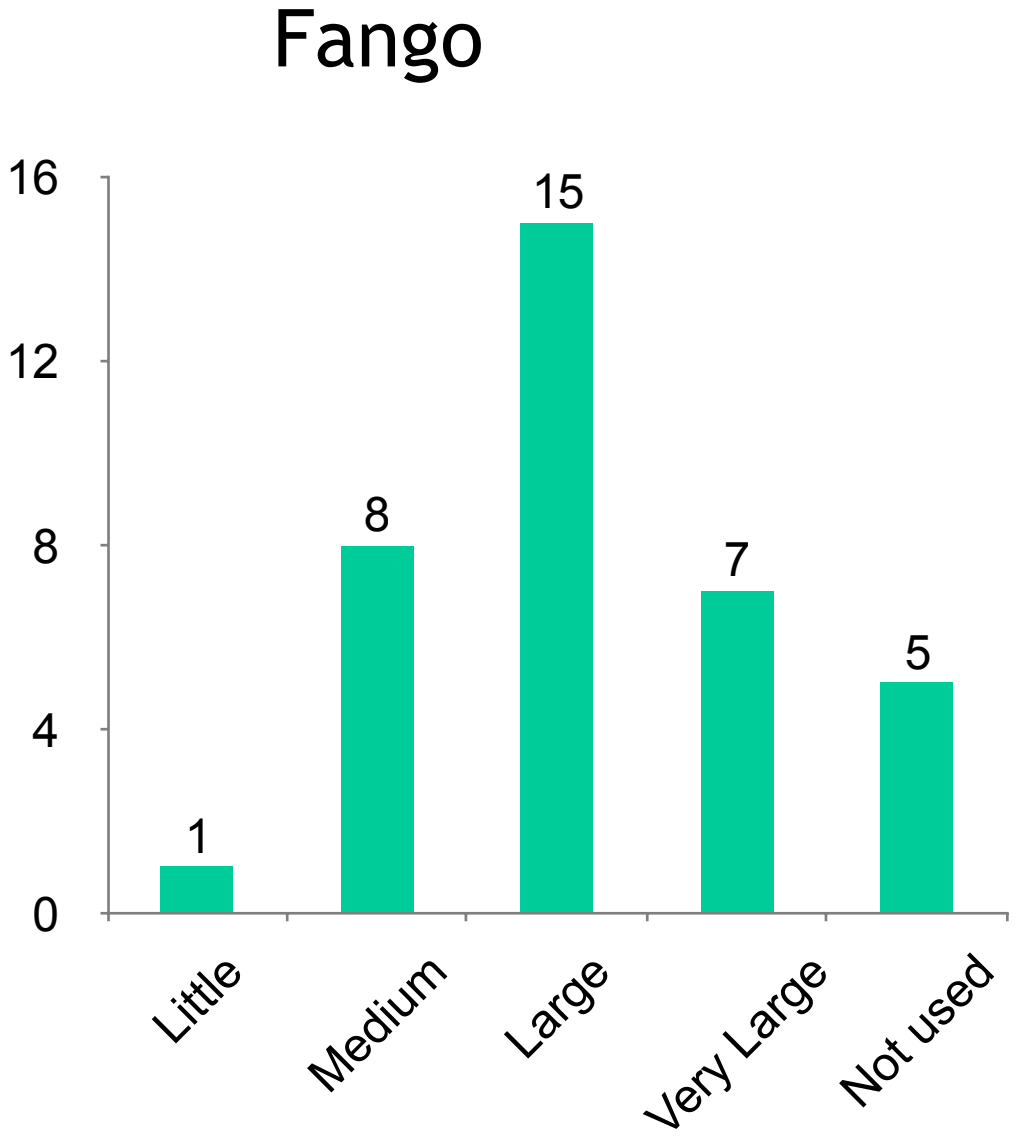
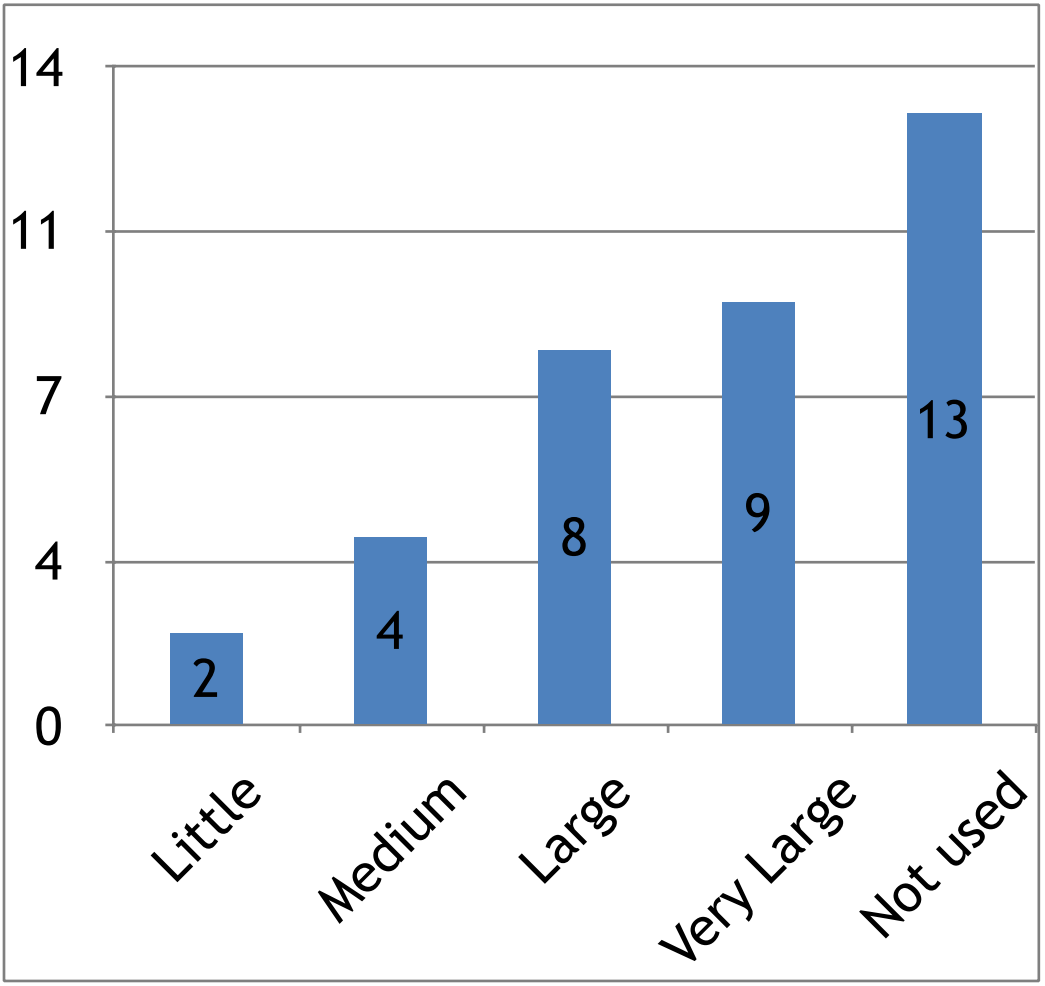




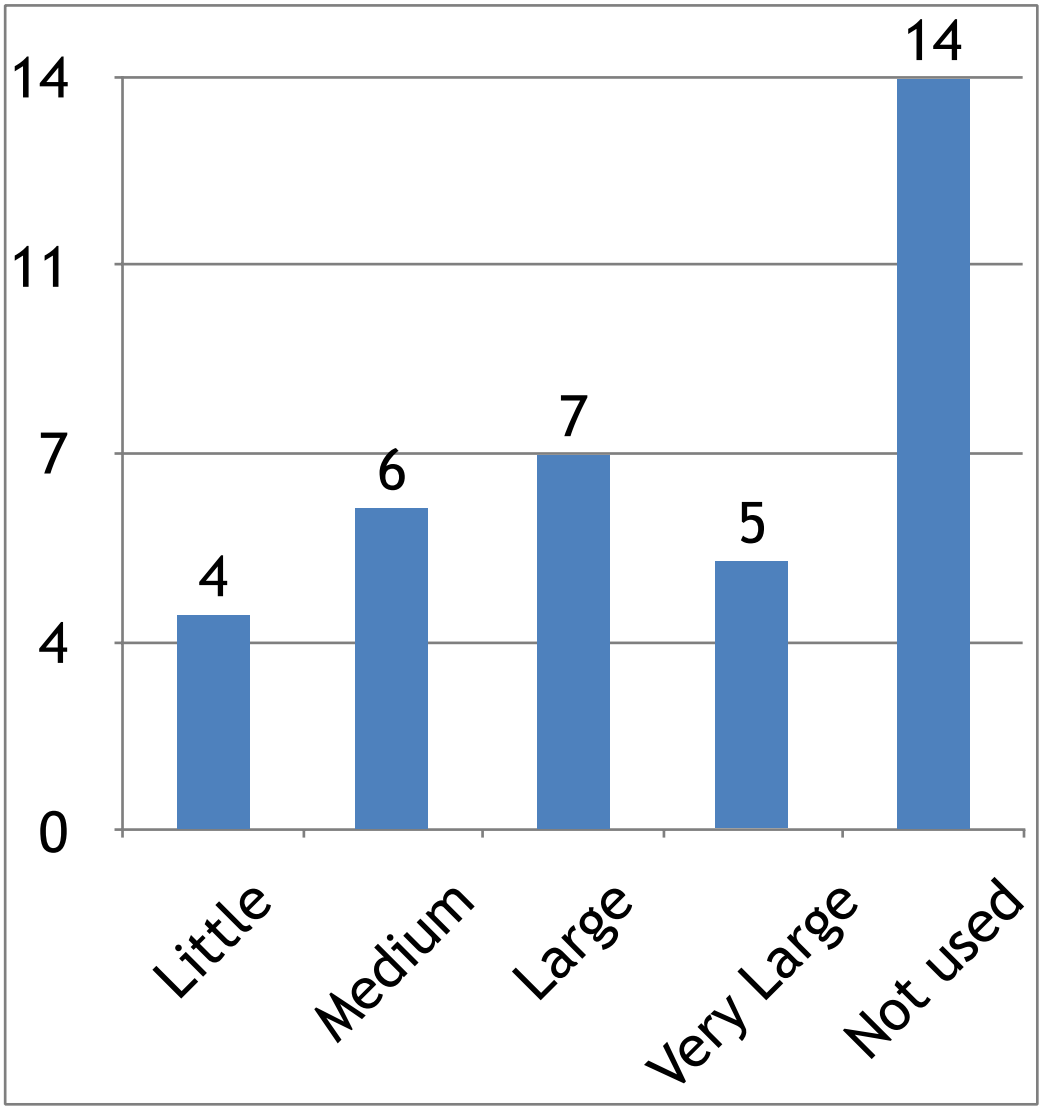
Effectiveness of natural remedies

Judged by Health resort physicians

Healthy Climate



Kneipp

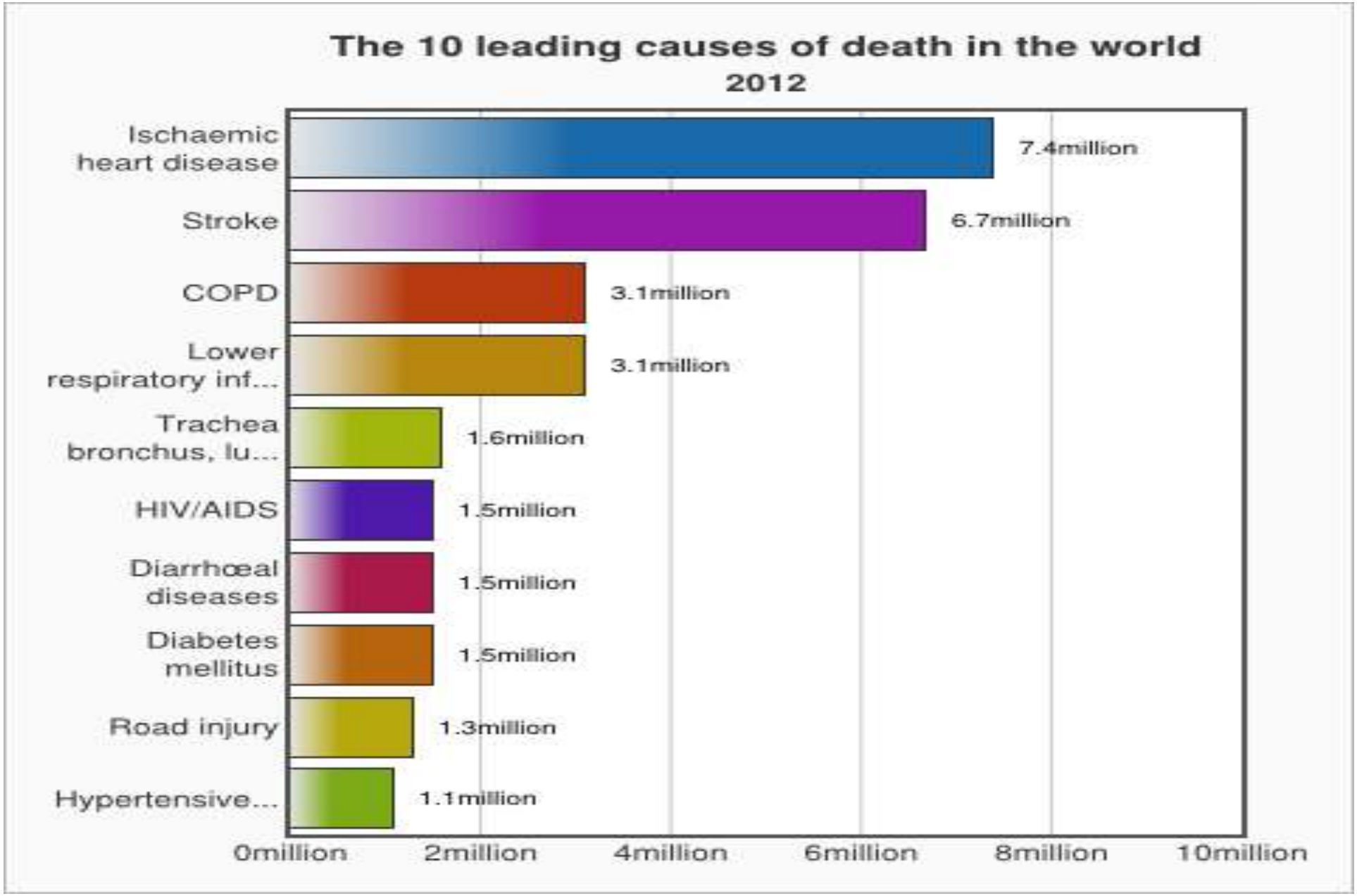


Health ressorts and Lifestyle change

Health ressorts are the ideal places

- High attraction
- High acceptance
- High adherence
- Long tradition of teaching and curing
- Experience with complex therapies for complex problems
- Salutogenetic principle

Chronic, lifestyle-related diseases



A Place for Health ressort medicine

•Acute and/or intense therapy: operation, syringes, ICU	• Hospitals
•	
•Intense, complex therapy for functional problems	• Rehabilitation clinics
•Intensity adapted complex therapy for complex problems, natural remedies and prevention	• **Health ressorts with Medicine and/or Medical Wellness**
•Minor problems, relaxation or activity is enough	• Holidays
•All kind of problems, before and after the other therapies	• Ambulant medicine (therapies at home)

Drinking water to prevent dementia

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Silicic acid and Alzheimer disease (AD)

Risk reduction with silicic acid in drinking water in 2 cohort trials from France between

11% for each **10 mg/day** more (n=3777)

36% for **> 12 mg/day vs < 12 mg/day** (n=383)

Main source for silicic acid **mineral water**

(silicic acid 8,8–35,7 mg/l),

Tap water contributed only with ca. 25%

(silicic acid 4,0–11,2 mg/l)

Water from Taketa (Naoiri) 230mg/l !

„Aluminum and silica in drinking water and the risk of Alzheimer's disease or cognitive decline: findings from 15-year follow-up of the PAQUID cohort". Rondeau et al. 2009. *American Journal of Epidemiology* 169 (4): 489–96.

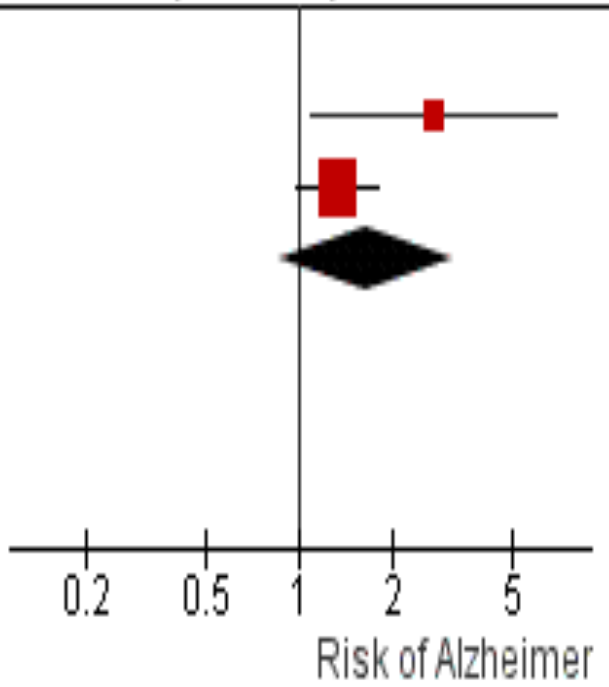
„Cognitive Impairment and Composition of Drinking Water in Women: Findings of the EPIDOS Study". Gillette-Guyonnet, et al 2005. *The American Journal of Clinical Nutrition* 81 (4): 897–902.

Meta-analysis silicic acid and AD

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.1.1 Silica				
Gillette-Guyonnet et al. 2005 (1)	1.008	0.4703	31.2%	2.74 [1.09, 6.89]
Rondeau et al. 2009 (2)	0.2852	0.1558	68.8%	1.33 [0.98, 1.81]
Subtotal (95% CI)			**100.0%**	**1.67 [0.86, 3.21]**

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 2.13$, df = 1 (P = 0.14); $I^2 = 53\%$

Test for overall effect: Z = 1.52 (P = 0.13)



Test for subgroup differences: Not applicable

(1) Silica intake ≤ 4 mg/d vs. > 12 mg/d vs.

(2) Silica intake ≤ 5.86 mg/d vs. > 15.45 mg/d vs.

Lithium and AD

2015 systematic review with meta-analysis

3 RCT n=232

Lithium significantly reduced mental decline of AD patients (SMD d = -0.41, 95% CI = -0.81 to -0.02, p = 0.04) (Matsunaga 2015).

This effect size is twice as large as the effect of approved drugs for the treatment of AD (Ströhle et al 2015).

„Lithium as a Treatment for Alzheimer's Disease: A Systematic Review and Meta-Analysis". Matsunaga, Shinji, Taro Kishi, Peter Annas, Hans Basun, Harald Hampel, und Nakao Iwata. 2015. Journal of Alzheimer's Disease: JAD 48 (2): 403–10.

„Drug and Exercise Treatment of Alzheimer Disease and Mild Cognitive Impairment: A Systematic Review and Meta-Analysis of Effects on Cognition in Randomized Controlled Trials". Ströhle, Andreas, et al. 2015. The American Journal of Geriatric Psychiatry 23 (12): 1234–49.

Lithium and AD

Microdoses of lithium (0.3 mg per day) for 15 months

reduced the mental decline of Alzheimer's patients small RCT

and in an animal model

„Microdose Lithium Treatment Stabilized Cognitive Impairment in Patients with Alzheimer's Disease". Nunes, Marielza Andrade, et al. 2013. *Current Alzheimer Research* 10 (1): 104–7.

„Chronic Microdose Lithium Treatment Prevented Memory Loss and Neurohistopathological Changes in a Transgenic Mouse Model of Alzheimer's Disease". Nunes, Marielza Andrade et al 2015. PLoS ONE 10 (11) https://doi.org/10.1371/journal.pone.0142267

Magnesium (Mg) and AD

- lower content of Mg of AD patients
  - in brain tissue (Glick 1990) (Andrási et al. 2005)
  - in the blood (Barbagallo et al. 2011)
  - in cerebrospinal fluid and hair (Veronese et al 2016)
- correlation of blood levels of Mg with the severity or the course of AD (Cilliler, Ozturk, and Ozbakir 2007)
- **But:** also elevated serum levels of magnesium in dementia (Kieboom et al., 2017)
- long-term increase in dietary magnesium intake has a positive influence on cognitive abilities (Cherbuin et al., 2014).
- case report: 2 x 500 mg magnesium daily dramatically improved the course of the disease for an AD patient temporarily (Glick and McMillan 2016).

Water analysis Naoiri (Kyushu, Japan)

Silicic acid 230 mg/l

Lithium 0,6 mg/l

Magnesium 268 mg/l

0,5 l per day fulfill the amount needed for prevention of AD

- Silicic acid 115 mg
  - 11%-risk-reduction for each 10mg
- Lithium 0,3 mg
- Magnesium 134 mg)

Thank you for your attention and let us work together

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